Belgian consensus guidelines for prostate core needle biopsy reporting

T. Gevaert, MD, PhD[1,2], L. Libbrecht, MD, PhD[3], E. Lerut, MD, PhD[4], B. Weynand, MD[4], M. Lammens, MD, PhD[5], S. Verschuere, MD, PhD[6], C. Mattelaer, MD[7], B. Lelie, MD[8], J. Eben, MD[9], L. Martinez, MD[10], M-A. van Caillie, MD[11], S. Rorive, MD, PhD[10,12], S. Verbeke, MD, PhD[13], M. Baldewijns, MD, PhD[5]

On behalf of the Belgian Working Group on Uropathology (BWGUP).

SUMMARY

The Belgian Working Group on Uropathology has agreed upon a dataset for prostate core needle biopsy reporting, based on existing international guidelines, recent scientific insights, national survey analysis and panel discussion, with the focus on a user- and receptor-friendly format. This dataset should encourage standardised structured reporting of prostate biopsies in the Belgian healthcare system, aiming to improve the quality of individual pathology reports and to provide real benefit for the clinical management of patients and secondary users. Therefore the Belgian Working Group on Uropathology recommends implementing this dataset in each Belgian pathology lab, in close consultation with the entire clinical team involved in the treatment of the prostate cancer patient.

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INTRODUCTION

Prostate cancer (PCa) is the most frequent tumour (23% of all cancers) and the third most important cause of cancer death in Belgian men.[1] The diagnosis of PCa is based on the microscopic evaluation of prostate tissue obtained through needle biopsy, and several evolutions in imaging and histopathological assessment have improved the diagnostic and clinical accuracy of this technique.[2] The most notable advance in biopsy-related imaging techniques has been multiparametric magnetic resonance imaging (MRI), which uses a specialised phase (e.g., diffusion-weighted, dynamic contrast-enhanced imaging) in addition to T2-weighted imaging.[3] On the histopathological level, there has been a major evolution with the recently introduced Grade Group (GG) system by the International Society for Uropathology (ISUP).[4-6] The GG system has been endorsed by the World Health Organization (WHO) and recognises five distinct grade groups based on the classic Gleason scoring (GS) system, with the advantage to offer a simplified and more straightforward classification with improved utility for therapeutic patient stratification.[4,7,8] The treatment of PCa has become increasingly complex over the past decades, and therapeutic decisions are often made

[1]Department of Pathology, AZ Klina, Brasschaat, [2]Organ Systems, KU Leuven, Leuven, [3]Department of Pathology, Université Catholique de Louvain, Brussels, [4]Department of Pathology, UZ Leuven, Leuven, [5]Department of Pathology, Universitair Ziekenhuis Antwerpen, Antwerpen, [6]Department of Pathology, AZ Delta, Roeselaere, [7]Department of Pathology, ZNA-ziekenhuizen, Antwerpen, [8]Department of Pathology, AZ Zeno, Knokke, [9]Department of Pathology, AZ Nikolaas, Sint-Niklaas, [10]Curepath, Jumet, [11]Department of Pathology, AZ Sint-Lucas, Brugge, [12]Department of Pathology, Université Libre de Bruxelles, Brussels, [13]Department of Pathology, UZ Gent, Ghent.

Please send all correspondence to: T. Gevaert, MD, PhD, Department of Pathology, AZ Klina, Augustijnslei 100, 2930 Brasschaat, Belgium, tel: +32478320422, email: gevaert.thomas1979@gmail.com.

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TABLE 1. Overview of the survey on prostate biopsies, as sent to the members of theThe Belgian Working Group on Uropathology BWGUP.

1. Which type of request form does your lab use for prostate biopsies: **Generic/Specific?**
2. Is the clinical information on the request form satisfactory: **Always/Mostly/Rarely/Never?**
3. Is the amount of cores per container provided: **Yes/No?**
4. Is the length of cores provided: **Yes/No?**
5. On how many levels is each core cut: **1/2/3/4?**
6. How many specimens (containers) are received?
7. How many cores are submitted in a single container?
8. Are cores being measured (wet) before embedding: **Yes/No?**
9. How is the reporting of positive biopsies done: **At the core level (per single biopsy)/At the specimen level (per container)/At the case level (per patient)/Combination of several options?**
10. Which grading system is used: **Gleason system/ISUP (WHO) system/Both?**
11. Are percentages of Gleason grade 4 and 5 included in the grading score: **Yes/No?**
12. Grading of a container with multiple cores: **Separate grading per core/Average grading?**
13. How is the grading provided in the summary of the report: **Separate grading per positive core/Separate grading per positive container/Overall grading/Composite score?**
14. Is the number of positive cores reported: **Yes/No?**
15. How is the extent of tumour in positive cores reported: **Percentage cancer/Cancer length/Combination?**
16. How is a discontinuous presence of cancer in a core reported: **By including the intervening benign tissue/By subtracting the intervening benign tissue/Combination of both?**
17. Is perineural tumour invasion reported: **Yes/No?**
18. Is invasion in periprostatic fat tissue reported: **Yes/No?**
19. Is lymphovascular invasion reported: **Yes/No?**
20. Is invasion in ejaculatory duct reported: **Yes/No?**
21. Is presence of intraductal carcinoma of the prostate (IDC-P) reported: **Yes/No?**
22. Is presence of cribriform carcinoma reported: **Yes/No?**
23. Is HGPIN reported in the absence of invasive carcinoma: **Yes/No?**

based on the input from a multidisciplinary team including surgeons, oncologists, radiologists and pathologists. In this context, reliable and high-quality prostate biopsy pathology reports are more and more mandatory to guide clinical decision making. There are several essential elements of quality in cancer pathology reporting: timeliness, accuracy, completeness, usability, conformance with current agreed standards, consistency and clarity in communication.[9,10] Several studies have shown that standardised structured reporting (SSR) using agreed published datasets significantly improves the quality of individual pathology reports as defined above.[9,10] The Canadian Ontario scale recognises six levels of reporting: level 1 follows a narrative model without defined content or formatting; level 2 uses a standardised content; level 3 integrates the standardised content in a structured lay-out; level 4 incorporates electronic reporting tools; and levels 5-6 incorporate equally fully structured electronic reporting with automatic coding, sophisticated data transfers into databases at the organisational level.[9,10] There is ample evidence that a higher Ontario scale provides benefit for the clinical management of patients and secondary users, like registries, research organisations, epidemiologists, etc.[9-12]

First attempts to introduce standardised reporting for prostate biopsies were already made some decades ago.[13] With the release of several guidelines and recommendations on prostate biopsy reporting in recent years (from the International Collaboration on Cancer Reporting [ICCR], College of American Pathologists [CAP] and ISUP), the international pathology community has shown an increased willingness to improve the quality of prostate biopsy pathology reports.[4,8,14-16] Recently, the Belgian Working Group on Uropathology (BWGUP) was founded under the auspices of the Belgian Society of Pathology (BSP). One of the strategic goals of the BWGUP is to improve the quality of uropathology reporting amongst the Belgian pathologists by providing datasets and encouraging and emphasising the use of standardised reports for the most frequent urinary and male genital cancers. This report presents our consensus dataset for prostate core needle biopsies. This dataset is based on and aligned to the existing international guidelines and recommendations (ICCR, ISUP, CAP, WHO and the European Association of Urology [EAU]), but the content is updated with recent scientific insights, and the format is adapted to the Belgian clinical and laboratory context.[4,7,8,14,15,17] This studies' major aim was to provide a dataset with evidence-based content in a user-friendly synoptic format, suitable for Ontario level 2-3 reporting.

METHODS

The different existing international datasets, guidelines and recommendations for prostate core biopsy pathology reporting (ICCR/WHO/CAP/ISUP/EAU) were reviewed.[4,7,14,15,17] An overview of all overlapping and non-overlapping parameters was made, and a survey with 23 multiple-choice questions on several critical parameters was sent to all members of the BWGUP (*Table 1*). A total of 13/19 BWGUP members responded to the survey, and the results were discussed and fine-tuned at multiple BWGUP meetings. A consensus was reached on the scientific content and lay-out for a Belgian prostate biopsy dataset.

DATASET

1. CLINICAL INFORMATION

- *Suspect area* (based on clinical examination and/or imaging): **YES** (please specify) / **NO**
- *Previous biopsy*: **YES** (please include date + Gleason Score/Grade Group) / **NO**
- *Previous therapy*: **YES** (please specify) / **NO**
- *Pre-Biopsy serum PSA*:
- *Clinical stage*:

2. MACROSCOPY

Specimen/container identification	Location	Total numbers of cores (n)	Length of cores (mm)

3. MICROSCOPY

Location	Length (mm)	Tumour	Type	GS	G4 (%)	GG	Extent (%)	Extent (mm)	Crib	IDC-P	EPE	HG-PIN/ ASAP
Apex Central (1)												

See explanatory notes for additional information.

4. SUMMARY

- *Tumour*: **YES** (specify special subtypes) / **NO**
- *Distribution*:
- *Number of positive cores/total number of cores*:
- *Highest Gleason score/Grade Group*:
- *IDC-P and/or Cribriform Carcinoma*: **YES** / **NO**

EXPLANATORY NOTES

1. CLINICAL INFORMATION

Correct and reliable clinical information has a significant impact on the diagnostic process and histopathological interpretation. Therefore, the BWGUP recommends using a standardised request form with a checklist of important clinical information, to ensure that clinicians provide all relevant clinical data needed for adequate histological diagnosis. The different parameters are based on the recent ICCR dataset for prostate core needle biopsy.[15]

2. MACROSCOPY

An optimised diagnostic prostate biopsy allows maximal cancer detection, avoidance of a repeat biopsy, increased likelihood of cancer detection during follow-up of men on active surveillance and adequate information for identifying men who need therapy and planning that therapy.[18-20] These goals are generally achieved through an 8-12 core systematic ultrasound-guided biopsy that incorporates apical and far-lateral cores in the template distribution, although newer techniques like MRI-targeted and transperineal template prostate biopsies have shown higher detection rates of significant and/or high grade PCa.[17-24] With the additional advantage of lower sepsis rates, these latter prostate biopsy approaches are expected to become the standard of care in the near future.[24]

The BWGUP recommends site-specific labelling and reporting (instead of laterality-based labelling and reporting). To avoid core fragmentation and to increase the likelihood of cancer detection, it is recommended not to pack more than two cores per container.[19] To optimise detection of small lesions, paraffin blocks should be cut at three levels.[7,17,25]

3. MICROSCOPY

- **Location**: Should be site-specific and as precise as possible.
- **Length**: Length of core (in mm) as measured on the glass slide.
- **Tumour**: Present or Absent.
- **Type**: Should be assigned in line with the 2016 WHO classification, and mixtures of different types should be indicated *(Table 2)*.[13]
- **GS**: Gleason Score.
- **G4 (%)**: Percentage of Gleason Grade 4*
- **GG**: Grade Group: should be assigned.[4,5]
- **Extent**: At least one measure of tumour extent should be provided (millimetres cancer length and/or percentage cancer in each core).*
- **Crib**: Cribriform Carcinoma: should be reported if present.*
- **IDC-P**: Intraductal Carcinoma of the Prostate: should be recorded if present.*
- **EPE**: Extraprostatic extension, Present or Not Identified.
- **HGPIN**: High-Grade Prostatic Intra-epithelial Neoplasia, and/or atypical small acinar proliferation (ASAP) should be reported in the absence of invasive carcinoma.

*Additional notes; see text.

GS/GG should be assigned at least per specimen or container.[8,14] If a specimen contains multiple cores, then an average score can be given for all grouped cores, unless the location of each core is specified by the urologist (i.e., by different colour inks) or if highly divergent grades are found.

The percentage of pattern 4 should be reported in GS7/GG2-3. [4,7,14,15] Knowledge of the percentage of pattern 4 in patients with GS7 can have an impact on patient care: patients with limited pattern 4 can be considered for active surveillance, and different radiation therapy approaches are available for Grade 3+4=7 versus Grade 4+3=7.[4] Increased percentage grade 4 correlates with increased risk of biochemical recurrence after radical prostatectomy (RP) and can improve prediction of upgrading the GS at the prostatectomy-specimen.[4]

The methods for the reporting of discontinuous PCa remain controversial.[15,16] Whether intervening benign tissue is included or subtracted from the extent measurement may determine eligibility for active surveillance.[15,16] Therefore, it is recommended that the tumour extent of a discontinuous cancer should be reported by both including and subtracting the intervening benign tissue, especially in clinically relevant cases.[15,16] In such cases an additional note can be included in the report, e.g., 'In a 20 mm core, there are discontinuous foci of GG 1 cancer spanning a distance of 12 mm (60% linear

TABLE 2. World Health Organization 2016 classification of invasive tumours of the prostate.

1. Epithelial tumours

- Acinar adenocarcinoma
  - Atrophic
  - Pseudohyperplastic
  - Microcystic
  - Foamy gland
  - Mucinous (colloid)
  - Signet ring-like cell
  - Pleomorphic giant cell
  - Sarcomatoid
- Ductal adenocarcinoma
  - Cribriform
  - Papillary
  - Solid

2. Neuroendocrine tumours

- Adenocarcinoma with neuroendocrine differentiation
- Well-differentiated neuroendocrine tumour
- Small-cell neuroendocrine carcinoma
- Large-cell neuroendocrine carcinoma

extent) and measuring 1+1 mm (10% linear extent)'.[15,16] Given the variability in criteria for reporting discontinuous foci of PCa in prostate biopsies, a close communication between pathologists and clinicians within a single institution is indicated to understand and align the clinical decision protocols for eligibility to active surveillance.

The presence of intraductal carcinoma of the prostate (IDC-P) should be recorded.[14,15] IDC-P is strongly associated with high volume, high-grade invasive PCa and metastatic disease, hence the presence of IDC-P in a biopsy, even if invasive carcinoma cannot be identified, mandates immediate repeat biopsy or definitive therapy (depending on the clinical situation).[14,15,26] It is important to distinguish IDC-P from high-grade prostatic intraepithelial neoplasia (HGPIN): compared to IDC-P, HGPIN has less architectural and cytological atypia and rarely a cribriform architecture.[15] There was a strong consensus at the 2014 ISUP consensus meeting that IDC-P should not be assigned a GG or GS.[6] Therefore, IDC-P should not be included in tumour extent measurements. Recent literature challenges several issues on IDC-P, so evolutions in the present recommendations can be expected in the near future.[27,28]

Although not yet endorsed by ICCR/CAP/ISUP (but included in the updated EAU guidelines), the BWGUP recommends including, routinely, the presence of cribriform PCa in the prostate biopsy pathology report.[17] In recent years, there has been compelling evidence in literature for an adverse prognostic impact of cribriform PCa.[29,30] Cribriform PCa is strongly associated with biochemical recurrence (BCR) and is an independent parameter for BCR after RP.[29,30] Presence of cribriform PCa is associated with metastasis, cancer specific death and p-stage.[30] Some studies have chosen to group cribriform PCa with IDC- P, a logical choice as most IDC-P is cribriform and as both lesions bear strong associations with adverse pathology.[30] Reporting the presence/absence of cribriform PCa in GG2 would be most crucial as men in this group with cribriform cancer should be excluded from active surveillance.[29,30]

4. SUMMARY

The existing prostate biopsy datasets (ICCR/CAP) do not contain a separate summary section.[14,15] It was the aim of the BWGUP to create a user- and receptor-friendly dataset, and we are convinced that a concise summary section is an essential part of this. Based on existing literature on the clinical and prognostic value of the different histopathologic parameters, the BWGUP recommends including the following elements in the summary section: presence/absence of tumour, distribution of tumour, number of positive cores/total number of cores, highest Gleason score/grade group and presence/absence of IDC-P and/or cribriform carcinoma. The number of positive cores and the percentage of positive cores are strong predictors of pathologic stage in RP.[16,31,32] The number of positive cores may be difficult to determine because of fragmentation, but packaging no more than two cores per container can help to overcome this.[15] Emerging data strongly suggest that a true volume measurement is more prognostic than pT2 substage.[33] Therefore, pathologically organ-confined disease is now considered pT2 in the eight edition of the American Joint Committee on Cancer (AJCC) tumour-node-metastasis (TNM) Staging Manual, and is no longer sub-classified by extent of involvement or laterality.[34] Although the overall image of the different GS is crucial for the clinical assessment of the patient with PCa, clinical decision making is often based on the highest GS.[4]

CONCLUSIONS

The BWGUP presents a consensus dataset for prostate core needle biopsy reporting, based on existing international guidelines, recent scientific insights and panel discussion. Recent prognostic pathologic parameters like cribriform carcinoma were included and a focus on a user- and receptor-friendly format was aimed for. In line with the increased international tendency to use SSR to improve quality of patient care, the BWGUP emphasises the clinical importance

KEY MESSAGES FOR CLINICAL PRACTICE

1. The Belgian Working Group on Uropathology (BWGUP) wants to encourage standardised structured reporting (SSR) of prostate biopsies in the Belgian healthcare system.
2. Therefore the BWGUP has developed a consensus dataset for prostate core needle biopsy reporting.
3. The BWGUP recommends to implementing the entire dataset in each Belgian pathology lab, in close consultation with the entire clinical team involved in the treatment of the prostate cancer patient.

of a wide use of this entire dataset in Belgian daily clinical practice.

In an initial phase, the implementation focuses on a standardised content of all prostate biopsy pathology reports, but in a later stadium the BWGUP aims to implement structured electronic reporting with automatic coding, sophisticated data transfers into databases and regular dataset updates. It is evident that a large-scale implementation of SSR of prostate biopsies in the Belgian healthcare system will only succeed by close interaction between pathologists, urologists, oncologists and other health care professionals.

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