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Clinical advantages in providing artificial intelligence-assisted prostate cancer diagnosis: A pilot study

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ABSTRACT

Prostate cancer is a prevalent male malignancy, with increasing incidence rates placing significant diagnostic burdens on pathology services worldwide. Artificial intelligence (AI) is emerging as a promising aid in enhancing diagnostic efficiency and accuracy. This study evaluates the clinical benefits of AI-assisted prostate biopsy (PB) diagnosis, with Paige Prostate tool, compared to non-AI-assisted PB diagnosis, focusing on its predictive accuracy for features in radical prostatectomy (RP) specimens. A retrospective analysis included 55 patients divided into two cohorts: one with non-AI-assisted PB diagnosis (n = 25) and another with AI-assisted PB diagnosis (n = 30). Pathological assessments recorded tumor size, Gleason score, Grade Group, and perineural invasion. The correlation between PB and RP results was analyzed, with statistical significance set at p < 0.05. AI-assisted PB diagnosis showed faster reporting times by 24 hours, enhancing workflow efficiency. AI assistance improved the correlation of tumor size between PB and RP, showing a substantial agreement (R=0.646, p < 0.001) compared to non-AI (R=0.479, p = 0.015). Gleason Score concordance increased by 13 % in the AI-assisted group, achieving 73.3 % versus 60 % in the non-AI-assisted group. This small pilot study suggests that AI-assisted PB diagnosis appears to enhance efficiency and accuracy in the diagnosis of prostate cancer, a finding to be confirmed with further studies.

1. Introduction

Prostate cancer is the most common cancer in men [1], with an estimated incidence in 2024 of 2–9 million cases [2], reflecting growing numbers that are difficult to prevent through lifestyle changes or public health measures alone [3]. This increasing incidence of prostate cancer, along with an increment in the complexity of diagnostic procedures, represents a growing workload for an already decreased pathologist workforce [4]. A comprehensive analysis of the worldwide distribution of pathologists demonstrates that measures need to be taken to face the depletion of these physicians responsible for the characterization of human diseases, based upon morphological and molecular-type data [4].

Our group previously demonstrated that the synergic use of the

artificial intelligence (AI) tool Paige Prostate in the pathological diagnosis of small prostatic biopsies (PBs) reduced reporting times by about 20 % [5]. In addition to this reduction in reporting times, our retrospective study could also demonstrate a reduction of nearly 40 % in second opinions and about 20 % fewer immunohistochemistry (IHC) requests [5].

Other groups could demonstrate that an AI-assisted PB diagnosis contributed to an increment in the diagnostic accuracy of prostate cancer as well as decreasing the interobserver variability [6–10]. These advantages, however, must be further examined, taking in consideration the associated costs and risks associated with the use of AI-assisted diagnosis [11].

Revisiting the idea that the ultimate gold standard in prostate cancer diagnosis is the systematic observation of the whole mount radical

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prostatectomy (RP) specimen [12], we decided to test the clinical impact of Paige Prostate AI-tool in predicting features of these specimens. In this retrospective study, we compare the ability of the PB diagnosis, performed with and without AI-assistance, to predict tumor size, Gleason score (GS), Grade Group (GrG) and percentage of pattern 4.

2. Material and methods

2.1. Case selection

Two cohorts of consecutive patients with prostate cancer, submitted to PB and followed by RP in the same institution, were selected. All specimens were originally reported by one of two senior pathologists (AP and JP).

Cohort 1 (C1) included 25 patients submitted to PB who, after a non-AI-assisted pathological diagnosis of prostate cancer, underwent RP. All whole slide images (WSIs) representing both PB and RP were reviewed in the digital archive of our institution. These specimens were registered between March 2021 and April 2023.

Cohort 2 (C2) included 30 patients submitted to PB who, after an AIassisted pathological diagnosis of prostate cancer, underwent RP. All WSIs representing both PR and RP were reviewed in the digital archive of our institution. These specimens were registered between May 2023 and May 2024, after validation and implementation of Paige Prostate AItool that was the tool used in the current study[5].

2.2. Pathological diagnosis and data collection

For each patient of each cohort, all prostate related (PB and RP) WSIs, both hematoxylin-eosin slides (HE) and IHC slides when available, were reviewed. The prostate biopsies were constituted by 4–12 fragments per container. Each container was labeled with the laterality and specific location if appropriate, and varied from 2 to 4, with no minimum tissue length restrictions. The review of the cases was performed by two pathologists (AA and JP), using CaseViewer (3DHISTECH, Ltd., Budapest, Hungary) in a 32-inches monitor (Sharp PN-K322BH, 3840 \times 2160 resolution) as for routine diagnosis [13] after scanning with the Pannoramic 1000 scanner (3DHISTECH, Ltd., Budapest, Hungary) at 20 \times magnification, with a protocol previously validated for primary diagnosis (pixel scale of 0.243 μ m/pixel).

For PB included in C2, the primary observation was performed using the FullFocus viewer and assisted by the FDA approved Paige Prostate AI-tool (Paige, New York, NY, USA), which was able to detect cancer, grading it, quantify tumor length and highlight perineural invasion. Paige Prostate is a deep learning-based AI tool, that has been previously described in detail [9]. Briefly, this AI system was trained using multiple instance learning, an approach that couples the WSIs with their corresponding diagnostic report, thus providing weak labels to each image. This approach does not require pixel level annotations and therefore permits using data at much larger scale than supervised methods.

In our practice, AI results are always integrated and interpreted by an expert pathologists, thus cultivating the synergic use, which is the intended use of Paige Prostate, and already recognized as the most beneficial use of AI tools in pathology [14]. This means that when the AI-tool is not completely in line with the pathologist's opinion, it is the opinion of the pathologist that prevails taking the result of AI into consideration. This fact is mentioned in the pathology reports of our institution.

The following parameters were retrieved from the digital records regarding patients included in both cohorts: age at diagnosis (years), time between PB and RP procedures (days).

The following parameters were retrieved from the digital archive for all PBs considering only the sample representing the dominant nodule (matching the respective RP topography as mentioned in the PB container): cancer histotype according to WHO, linear tumor size, Gleason score (GS), Grade Group (GrG), percentage of pattern 4, presence of perineural invasion and turnaround time (time from registration to signing out the report).

The following parameters were retrieved from the digital archive for all RPs considering only the sample representing the dominant nodule: cancer histotype according to WHO, tumour size, GS, GrG, percentage of pattern 4, presence of perineural invasion and TNM (AJCC, 8th edition). All RPs were observed after a whole mount sampling.

2.3. Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 27.0 for Windows (IBM). Pearson's chisquared (χ 2) test (or Fisher's exact test when applicable) was used for comparison of qualitative variables, and the Mann–Whitney (MW) test, and the Kruskal–Wallis (KW) test was used for comparison of quantitative variables. The Pearson test was used for correlation analysis. The level of significance was set at p < 0.05. Concordance rates were evaluated with simple (diagnostic concordance) and quadratic weighted kappa (QWK) statistics to penalize discordances with higher clinical impact. The Landis and Koch classification was used to interpret the values: no agreement to slight agreement (< 0.20), fair agreement (0.21–0.40), moderate agreement (> 0.81).

3. Results

This study included 55 patients with prostate cancer divided into two cohorts, C1 and C2. C1 comprehended 25 patients with a median age of 67 years-old (range: 52–78 years old) at the time of diagnosis, and C2 comprehended 30 patients with a median age of 68 years old (range 51–77 years old) at the time of diagnosis, as described in Table 1. All PBs included in both cohorts had a diagnosis of acinar adenocarcinoma, and the same holds true for all the RP specimens included in both cohorts, indicating that there were no false positive PB diagnoses.

The median time between the PB procedure and the RP was 13 days less in C2 (median time 44 days) than in C1 (median time 57 days), although without significant statistical meaning (MW, p = 0.155) (Table 1). The time for reporting PB was faster in C2 (mean time 48 working hours) in comparison with C1 (72 working hours) (MW, p = 0.002), representing a 24-hour gain (1 day). All the other features related to tumor size, grading and TNM were similar among cohorts (Table 1). There were no records of T1, T4 or M1 disease in our pilot series.

In terms of the ability of the PB to predict the findings in the RP, considered to be the gold standard, both cohorts were compared.

The linear cancer size measure within a PB with AI-assistance in C2 correlates better (substantial agreement) with the largest size of the dominant nodule (R=0.646; p < 0.001) than the measures taken without AI-assistance in C1 (moderate agreement) (R=0.479, p = 0.015) (Fig. 1).

All PBs that disclosed perineural invasion had this finding also present in the correspondent RP, in both cohorts (all 5 cases). In none of the cohorts it was possible to accurately predict the presence of perineural invasion in RP due to the low frequency of this finding in PB.

Table 2 summarizes the ability of PB grading in predicting the respective RP grading, in both cohorts. With the help of AI assistance, it is possible to predict grading more accurately in 13 % of cases. The GS concordance between PB and RP was 60 % in C1 and was 73.3 %. The GS6 evaluation PB is more accurate in 27 % of the cases (11 % and 38 % matching GS6 in PBs and respective RPs, without and with AI-assistance, respectively). The GS7 evaluation is also more accurate in 13 % of the cases (87 % and 100 % matching GS7 in PBs and respective RPs, without and with AI-assistance, respectively). The PB cancer diagnosis with the help of AI fails to predict GS8 although the analysis is based in scant cases.

Regarding the GrG, the concordance between PB and RP evaluations for GrG1, improves 27 % with the help of AI, but AI fails to improve the

Table 1

Clinical and pathological features of the 2 cohorts.

	Cohort 1 Non-AI- assisted diagnosis PB	Cohort 2 AI-assisted diagnosis PB	p value
Number of patients	25	30	n.a.
Age of the patient (years, median [P25–P75])	67 [62;71]	68 [59;71]	p = 0.660*
Time between PB and RP (running days, median [P25; P75])	57 [44;70]	44 [37;66]	p = 0.155*
Time for reporting PB (hours in working days, [P25; P75])	72 [50;90]	48 [27;53]	p = 0.002*
Linear cancer size of dominant nodule in PB (mm, median [P25; P75])	17.8[4.0;31.4]	16.6 [8.7;26.2]	p = 0.692*
Larger diameter of the dominant nodule in RP (mm, median [P25; P75])	15.0 [11.0;21.0]	15.0 [13.0;20.0]	$p = 0.972^{*}$
Presence of perineural invasion in PB (n; %)	2; 8.0	3; 10.0	p > 0.999**
Presence of perineural invasion in RP (n; %) GS/GrG of dominant nodule in PB (n: %)	22; 88.0	25; 83.3	$p = 0.715^{**}$
6 (3 +3)/GrG1	9: 36.0	8: 30.0	p = 0.178***
7(3 + 4)/GrG2	5: 20.0	14: 43.3	(GrG1/2 vs GrG3/
7(4 +3)/GrG3	10; 40.0	5; 20.0	4/5)
8(4 +4)/GrG4	1; 4.0	3; 6.7	
9(4 +5)/GrG5	0; 0.0	0; 0.0	
GS/GrG of dominant	1; 4.0	3;10.0	p = 0.551***
nodule in RP (n; %)	12;48.0	15; 50	(GrG1/2 vs GrG3/
6 (3 +3)/GrG1	9;36.0	11; 36.7	4/5)
7(3 +4)/GrG2	2; 8.0	0; 0.0	
7(4 +3)/GrG3	1;4.0	1; 3.3	
8(4 +4)/GrG4			
9(4 +5)/GrG5			
Percentage of pattern 4 in dominant nodule in PB (median [P25; P75])	40 [0;65]	20[0;60]	p = 0.823*
Percentage of pattern 4 in dominant nodule in RP (median [P25: P75])	45 [18;75]	30[5;63]	p = 0.206*
TNM classification in RP			
(II, %) T2	20.80.0	20.667	n = 0.960***
12 T22	20, 80.0 4: 16.0	20,00.7	p = 0.900
T3b	1:40	2:66	
Nx	8: 32.0	4: 13.3	$p = 0.269^{***}$
NO	17: 68.0	25: 83.4	r ollos
N1	0: 0.0	1: 3.3	
R0	14	17; 56.7	p > 0.999**
R1	11	13; 43.3	•

Legend: PB, prostate biopsy; RP, radical prostatectomy; AI, artificial intelligence; P, percentile; GS, Gleason Score; GrG, Grade Group; * Mann-Whitney test; ** Fisher's exact test; ***Chi-square test; n.a. – not available.

GrG evaluation in PB in comparison with RP in more severe GrGs. Also, according to these results, the evaluation of pattern 4 in PB in comparison with the respective RP does not improve with the AI-assistance (C1 – R=0.821; p < 0.001; C2 – R=0.693; p < 0.001).

4. Discussion

In the setting of prostate cancer, the previously reported advantages of AI-assisted diagnosing in PB diagnosis include an increase in efficiency, accelerated reporting, and fewer second opinion and IHC requests[5], as well as improved accuracy and interobserver concordance [6–8]. In the present pilot study, based upon analysis of a single clinical setting, we demonstrate that with the help of an AI-tool it is possible to

report the prostate cancer diagnosis 24 hours earlier when compared with a non-assisted diagnosis. An improved turnaround time for diagnosis of the PB can decrease patients' anxiety on this subject and ultimately accelerate treatment decisions. In the work hereby reported we could not demonstrate that the patients included in C2, who were receiving the diagnosis of cancer earlier, were submitted to RP significantly faster. However, the median time until surgery was reduced by 13 days. The single institution enrolled in our study does not recommend RP less than 4 weeks after the PB, as a protocol, limiting the impact of these calculations. Here, the authors recognize that other variables not controlled by our study may influence the time between the PB and the RP, namely availability of surgery rooms and/ or personnel. The fact is that the two cohorts were consecutive in time (starting in 2021 and ending in 2024), representing enough room for modifications in the patient journey planning at the clinical level that were not controlled by pathologists. Most importantly, the patients and their physicians were aware of the diagnosis significantly earlier in C2, and they were able to plan RP in advance if required.

Regarding the increment in accuracy, our group could not demonstrate this advantage with the use of Paige Prostate in a previous study, testing the performance of 4 experienced pathologists diagnosing with and without the help of AI, since the baseline performance of the pathologists enrolled in this prior study was already very high. [5]. Nevertheless, we concluded that the AI-tool was functioning, in practical terms as a second opinion that allowed us, in that study, to decrease by nearly 30 % the diagnosis of atypical small acinar proliferation and, as per consequence, the level of uncertainty [5]. Another question to consider is whether the increment in interobserver concordance is a real benefit of the use of AI since we are understanding today that AI-driven bias may lead to inadequate agreement with AI-tool results in everyday practice [11] and that AI-tools do not agree totally with each other when performing the same task [15].

In the current study we understood that the benefits of using an AItool such as Paige Prostate for guiding the observation of PB may have advantages that go beyond efficiency. In the retrospective and comparative pilot study herein described, we demonstrate that the AIassisted diagnosis of prostate cancer may better predict some of the features of the RP, possibly allowing a more precise planning of the treatment of the disease in comparison with a non-assisted observation.

In the current study, we demonstrate that the AI-assisted prostate cancer diagnosis allows a better correlation between the cancer linear size in PB and RP in the same dominant nodule. This result may help the clinician/surgeon to better predict the extension of the tumor and to plan the surgery accordingly. Although our analysis was performed in samples collected at the same institution, it was not possible to determine whether the operator that performed the PB to the patient was the same, or if technical conditions were not modified. We acknowledge that the technical procedure influences the quality of the sample and that this may constitute a limitation of this study, together with the small size of the series. Nevertheless, the mean linear cancer size in both cohorts was considered similar, providing indirect evidence about the maintenance on the quality standards of the sampling procedure among cohorts. Another feature that is influenced by the sampling is perineural invasion. PB diagnosis fails to predict the presence of perineural invasion in RP even with the help of AI in our study, a finding that may also be justified by the small number of cases in the series.

It was already reported in the literature that the evaluation of the GS in PB tends to underestimate the GS detected in RP, depending on the size of the PB [16,17]. In our study, we demonstrate that AI-assisted observation of prostate cancer in PBs has also advantages in predicting more accurately the GS of RPs in about 13 % more cases in comparison with a non-assisted AI-observation. This better prediction will be essential to better planning for the treatment of these patients. The impact of this observation can only be fully assessed in clinical studies with larger cohorts of patients that include the follow-up information.

The prediction of the GrG1 in RP with the help of AI improves in



Fig. 1. Correlation between the linear cancer size measured in the prostate biopsy (PB) and the largest diameter of the dominant nodule in radical prostatectomy (RP), evaluated without (A) and with AI-assistance (B).

Table 2

Correlation between PB grading and RP grading in both cohorts.

Cohort 1 Non AI-assisted diagnosis PB			Cohort 2 AI-assisted diagnosis PB GS of dominant nodule in PB			
GS of dominant nodule in PB						
6 7	8	9	6	7	8	9
1 0	0	0	3	0	0	0
8 13	0	0	5	19	2	0
0 1	1	0	0	0	0	0
0 1	0	0	0	0	1	0
11 % 87 %	100 %	n.a.	38 %	100 %	0 %	n.a.
GS concordance between PB and respective RP in 60.0 % of cases;			GS concordance between PB and respective RP in 73.3 % of cases;			
Quadratic weighted kappa 0.313			Quadratic weighted kappa 0.547			
GrG of dominant nodule in PB			GrG of dominant nodule in PB			
1 2	4	5	1	3	4	5
	3		2	2		
1 0	0 0	0	3 0	0 0	0	0
7 4	1 0	0	5 8	3 2	0	0
1 1	7 0	0	0 6	5 3	2	0
0 0	1 1	0	0 0	0 0	0	0
0 0	1 0	0	0 0	0 0	1	0
11 % 80 %	100 %	n.a	38 %	60	% 0%	n.a.
70 %			57 %			
GrG concordance between PB and respective RP in 52.0 %; Quadratic weighted kappa 0.612			GrG concordance between PB and respective RP in 46.7 %;			
			Quadratic weighted kappa 0.651			
	Johort 1 Jon AI-assisted d SS of dominant n SS of dominant n 0 1 0 1 1 % 87 % SS concordance b Quadratic weight Go dominant 2 0 1 % 87 % SC concordance b Quadratic weight 2 0 4 0 1 % 80 % GrG concordance Quadratic weight	Johort 1 Jon AI-assisted diagnosis PB SS of dominant nodule in PB SS of dominant nodule in PB 0 0 13 0 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 1% 87 % 100 % Sconcordance between PB and res Quadratic weighted kappa 0.313 GG of dominant nodule in PB 2 4 3 0 0 4 1 0 0 1 7 0 1 0 1 0 1 0 1 0 1 0 1 0 0 1 0 0 1 0 0 1 0 0 0 100 % 70 % </td <td>Johort 1 Son AI-assisted diagnosis PB So of dominant nodule in PB 0 0 13 0 0 1 0 0 13 0 0 1 0 0 14 1 0 0 15 0 16 7 17 0 0 0 18 87 % 100 % n.a. 65 3 37 4 18 5 3 3 38 3 39 3 39 3 39 3 30 0 30 0 39 3 39 3 30 0 4 1 0 0 1 0 1 0 1 0 1 0 1 <t< td=""><td>Cohort 1 Cohort 2 Ion AI-assisted diagnosis PB AI-assisted So of dominant nodule in PB GS of dom 0 0 0 0 1 0 0 0 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 0 0 0 1 0 0 0 1 0 0 0 1 0 0 0 1 0 0 0 2 4 5 1 2 4 5 1 3 0 0 0 0 2 4 5 1 2 4 1 0 0 0 0 <td>Cohort 2AI-assisted diagnosis PBAI-assisted diagnosis PSS of dominant nodule in PBGS of dominant nodule000110010110010100100100100100100100100100100100100100000100000100245302430301024303041001001001000100010001000100010001000100010000000<</td><td>Cohort 1 Cohort 2 AI-assisted diagnosis PB So of dominant nodule in PB So concordance between PB and respective RP in 60.0 % of cases; Quadratic weighted kappa 0.313 CrG of dominant nodule in PB 2 4 2 4 Quadratic weighted kappa 0.313 CrG of dominant nodule in PB CrG of dominant nodule in PB CrG of dominant nodule in PB 2 4 2 4 2 2 3 0 2 4 2 2 2 2 3 0 2</td></td></t<></td>	Johort 1 Son AI-assisted diagnosis PB So of dominant nodule in PB 0 0 13 0 0 1 0 0 13 0 0 1 0 0 14 1 0 0 15 0 16 7 17 0 0 0 18 87 % 100 % n.a. 65 3 37 4 18 5 3 3 38 3 39 3 39 3 39 3 30 0 30 0 39 3 39 3 30 0 4 1 0 0 1 0 1 0 1 0 1 0 1 <t< td=""><td>Cohort 1 Cohort 2 Ion AI-assisted diagnosis PB AI-assisted So of dominant nodule in PB GS of dom 0 0 0 0 1 0 0 0 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 0 0 0 1 0 0 0 1 0 0 0 1 0 0 0 1 0 0 0 2 4 5 1 2 4 5 1 3 0 0 0 0 2 4 5 1 2 4 1 0 0 0 0 <td>Cohort 2AI-assisted diagnosis PBAI-assisted diagnosis PSS of dominant nodule in PBGS of dominant nodule000110010110010100100100100100100100100100100100100100000100000100245302430301024303041001001001000100010001000100010001000100010000000<</td><td>Cohort 1 Cohort 2 AI-assisted diagnosis PB So of dominant nodule in PB So concordance between PB and respective RP in 60.0 % of cases; Quadratic weighted kappa 0.313 CrG of dominant nodule in PB 2 4 2 4 Quadratic weighted kappa 0.313 CrG of dominant nodule in PB CrG of dominant nodule in PB CrG of dominant nodule in PB 2 4 2 4 2 2 3 0 2 4 2 2 2 2 3 0 2</td></td></t<>	Cohort 1 Cohort 2 Ion AI-assisted diagnosis PB AI-assisted So of dominant nodule in PB GS of dom 0 0 0 0 1 0 0 0 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 0 0 0 1 0 0 0 1 0 0 0 1 0 0 0 1 0 0 0 2 4 5 1 2 4 5 1 3 0 0 0 0 2 4 5 1 2 4 1 0 0 0 0 <td>Cohort 2AI-assisted diagnosis PBAI-assisted diagnosis PSS of dominant nodule in PBGS of dominant nodule000110010110010100100100100100100100100100100100100100000100000100245302430301024303041001001001000100010001000100010001000100010000000<</td> <td>Cohort 1 Cohort 2 AI-assisted diagnosis PB So of dominant nodule in PB So concordance between PB and respective RP in 60.0 % of cases; Quadratic weighted kappa 0.313 CrG of dominant nodule in PB 2 4 2 4 Quadratic weighted kappa 0.313 CrG of dominant nodule in PB CrG of dominant nodule in PB CrG of dominant nodule in PB 2 4 2 4 2 2 3 0 2 4 2 2 2 2 3 0 2</td>	Cohort 2AI-assisted diagnosis PBAI-assisted diagnosis PSS of dominant nodule in PBGS of dominant nodule000110010110010100100100100100100100100100100100100100000100000100245302430301024303041001001001000100010001000100010001000100010000000<	Cohort 1 Cohort 2 AI-assisted diagnosis PB So of dominant nodule in PB So concordance between PB and respective RP in 60.0 % of cases; Quadratic weighted kappa 0.313 CrG of dominant nodule in PB 2 4 2 4 Quadratic weighted kappa 0.313 CrG of dominant nodule in PB CrG of dominant nodule in PB CrG of dominant nodule in PB 2 4 2 4 2 2 3 0 2 4 2 2 2 2 3 0 2

Legend: PB, prostate biopsy; RP, radical prostatectomy; AI, artificial intelligence; GS, Gleason Score; GrG, Grade Group, n.a. - not available.

27 % of cases. This finding may have important clinical implications, since one of the main objectives of prostate cancer screening is to separate patients with clinically significant disease (usually GrG2 and above) from those in GrG1, who typically have a more indolent course [18]. Therefore, AI-assisted PB diagnosis may serve to better identify patients that are candidates for active surveillance programs as opposed to active treatment, with the consequent reduction in morbidity, mortality and associated healthcare costs that may derive from unnecessary treatment.

Despite this important finding, the synergic use of AI was not able to improve the prediction of more severe GrG in our study. This is probably due to a difficulty in the evaluation of pattern 4 in PB that it is not optimal when pathologist evaluates PB material even with the help of AI. Further studies and perhaps enhanced AI detection of pattern 4 may eventually help overcome this limitation. In previous studies [15], the performance of Paige Prostate tends to have a less good performance in GrG3,4 and 5, and a great performance in separating benign from low grade cancers, indicating that this software is mainly trained to be very sensitive in flagging cancer in a sample, more than stratifying rare high-grade cancers.

For some years now, our group has reported on how working in synergy with AI-tools provide significant advantages to the performance and comfort of the pathologist [14]. In this work we provide arguments that go beyond the pathology realm and have the potential to translate into clinical benefits for the patient. The results herein presented may also contribute to justify the, so called, business case of the AI-assisted diagnosis in pathology. These potential benefits, highlighted by this small pilot study, include a faster diagnosis, and a better prediction of both the dominant nodule size and GS, for more precise patient management. These findings should be supported by further studies, with larger series that may overcome the limitations of the small sample size herein reported, that restrict the generalizability of the findings, and the statistical power to detect differences, particularly for less frequent findings. This pilot highlights the advantages of using AI particularly for those GrG1 patients that are better placed in active surveillance programs and avoid unnecessary overtreatment and its consequences.

CRediT authorship contribution statement

Antonia Syrnioti: Data curation. António Polónia: Writing -

review & editing, Validation, Formal analysis. **Rui Prisco**: Validation, Conceptualization. **Alexandra Asaturova**: Writing – original draft, Data curation. **Catarina Eloy**: Writing – review & editing, Validation, Supervision, Investigation, Conceptualization. **Ivan Rienda**: Data curation. **João Pinto**: Supervision, Formal analysis, Data curation, Conceptualization.

Compliance with ethical standards

Formal ethical approval was not required for this study, as it was a retrospective study based upon archive material only, without any implication to the direct patient care of the enrolled cases; performed in accordance with the Declaration of Helsinki.

Contributions

CE, JP and RP designed the study; CE and AA wrote the document; AA, IR, AS and JP collected data; AA and JP did review of the specimens; AA and AP performed statistical analysis. All authors reviewed and approved the final manuscript

Author statement

Here we re-submit our work "Clinical advantages in providing artificial intelligence-assisted prostate cancer diagnosis: a pilot study".

All authors consent in this reviewed submission.

We hope that you find our pilot study innovative and valuable to be accepted for publication.

Declaration of Generative AI and AI-assisted technologies in the writing process

Generative AI: was not used

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Catarina Eloy reports a relationship with Merck Sharp & Dohme UK Ltd that includes: consulting or advisory. Catarina Eloy reports a relationship with Sakura that includes: speaking and lecture fees. Catarina Eloy reports a relationship with Diapath that includes: speaking and lecture fees. Catarina Eloy reports a relationship with Diaceutics that includes: speaking and lecture fees. Catarina Eloy reports a relationship with Biocartis that includes: consulting or advisory. Antonio Polonia reports a relationship with Indica Labs that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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