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Pathology

Evaluating Conventional Light Microscopy for Primary Diagnosis of Prostate Lesions: A Validation Study on Small Biopsy Specimens

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Abstract **Original Research Article**

Prostate biopsies are crucial for diagnosing prostate lesions, including cancer. The procedure typically involves obtaining tissue samples using a needle. While the severity of complications is generally low, common adverse effects include mild bleeding, infection, and discomfort. Severe complications are rare. The incidence of clinically significant prostate cancer detection through core biopsies is significant, making it an indispensable diagnostic tool. The biopsies are traditionally viewed on glass slides by Conventional Light Microscopy (C.L.M.). Whole Slide Imaging (WSI): Whole Slide Imaging (WSI) involves scanning entire glass slides to produce high-resolution digital images. These images can be viewed, analysed, and shared electronically, enabling remote consultation and diagnosis. ***Aim:*** To assess the diagnostic accuracy of WSI compared to CLM. ***Material and methods:*** This single-center, cross-sectional study assessed diagnostic concordance in prostate lesion biopsies using Conventional Light Microscopy (CLM), with evaluations by two pathologists. It included core, tru-cut, and sextant biopsies, focusing on CLM accuracy. Inclusion criteria covered all available prostate biopsy specimens, while exclusion criteria included inadequate samples or those unsuitable for analysis. Selective sampling ensured a representative distribution of various prostate lesions. ***Results:*** The table shows diagnostic concordance and discrepancies between two pathologists using Conventional Light Microscopy (CLM) for prostate biopsies. While there was strong agreement in benign cases like BPH, differences were noted in adenocarcinoma grading, Gleason scores (G.S.), and perineural invasion (PNI). Some cases showed variations in Gleason pattern interpretation, affecting final diagnoses. These findings highlight inter-observer variability, suggesting the need for further analysis, possibly incorporating Whole Slide Imaging (WSI) to improve diagnostic consistency. ***Conclusion:*** This study aims to elucidate the potential and validate the efficacy of Whole Slide Imaging in the realm of pathological diagnostics, specifically focusing on its application in the primary diagnosis of prostate lesions through the analysis of small biopsy specimens. WSI is comparable to CLM and can be safely incorporated for primary histological diagnosis of prostate core biopsies.

Keywords: CLM, WSI, porstate, specimen.

INTRODUCTION

Prostate biopsies play a critical role in diagnosing prostate lesions, including malignancies, by providing histological evidence of disease presence and severity. The procedure involves extracting small tissue samples using a core needle, typically guided by ultrasound. While generally safe, it may cause mild complications such as bleeding, infection, or discomfort, though severe adverse effects are rare.

Core biopsies remain an essential tool in detecting clinically significant prostate cancer, as they help determine tumor grade, extent, and aggressiveness. The conventional method of examining prostate biopsy samples involves viewing tissue sections on glass slides using Conventional Light Microscopy (CLM). CLM remains the gold standard for pathological evaluation, allowing direct morphological assessment by trained pathologists. However, this method has limitations, including issues related to slide storage, deterioration, and accessibility for remote consultations.

CLM in prostate biopsies remains a subject of ongoing research, necessitating validation studies to ensure reliability in clinical practice. W.S.I. provides an

accurate and reliable alternative to traditional light microscopy, ensuring comparable diagnostic precision for pathologists. It enhances workflow efficiency by enabling remote access and minimizing the need for physical slide handling. Additionally, W.S.I. supports education and research by allowing easy sharing of slides and annotations, fostering collaboration and learning. So present study was carried out to validate the results.

Aim: To assess the diagnostic accuracy of WSI compared to CLM.

MATERIAL AND METHODS

This single-center, cross-sectional observational study aimed to evaluate diagnostic concordance between Conventional Light Microscopy (CLM) and WSI in prostate lesion biopsies, with assessments conducted by two pathologists. The study included various prostate lesions diagnosed through core, tru-cut, and sextant biopsies, focusing on the accuracy of CLM. Each biopsy specimen was analyzed using CLM methods, and the results were calculated. Inclusion: All biopsy specimens from prostate lesions available for both WSI and traditional microscopic analysis. Exclusion: Specimens with inadequate tissue samples or those unsuitable for scanning due to technical limitations. Selective sampling was employed to ensure a representative distribution of various prostate lesions.

Sixty-one prostate core biopsy slides from 14 cases, reported between January 2023 and June 2024, were scanned using the Optra Scan OS-Lite whole slide imaging scanner, which provides bright-field visualization up to 40x resolution. Each image was uniquely identified, archived, and analyzed using Optra Scan's proprietary software. The scanned images, saved as JP2 files, ranged from 0.111 GB to 0.890 GB, with the largest case consuming 2.5 GB and total data usage reaching 25.6 GB. The files were viewable using Optra Scan's software, allowing 40x magnification. Data, including patient history, PSA values, radiological findings, and diagnostic findings were recorded in Excel.

Validation procedure: Two pathologists independently evaluated 61 core biopsies, first using conventional light microscopy (CLM). They assessed overall diagnosis (benign or malignant), specific pathology, perineural invasion (PNI), lymphovascular invasion (LVI), and, in cases of prostatic adenocarcinoma, Gleason score (GS) and Grade Group (GG) per WHO 2022 guidelines. Data, including patient demographics, lesion characteristics, and diagnostic outcomes, were collected in Excel.

RESULTS

Table 1: 14 cases and their interobserver and intraobserver correlations when viewed by 2 independent pathologists for WSI and CLM along with the final diagnosis

Sr. No	Final diagnosis	Pathologist 1	Pathologist 1	Pathologist 2	Pathologist 2
		WSI diagnosis	CLM diagnosis	WSI diagnosis	CLM diagnosis
1	Adenocarcinoma, G,G-5, G.S.5+4=9 PNI +	Adenocarcinoma, G.S 5+4=9	Adenocarcinoma G.S. 5+5=10	BPH	Adenocarcinoma, G.G. 5, G.S.5+4=9 PNI +
2	BPH with focal epithelial hyperplasia	BPH	BPH	BPH with acute on chronic prostatitis	BPH with focal epithelial hyperplasia
3	BPH with BCH	BPH with CP with atrophy	BPH with CP	BPH with prostatitis	BPH with BCH
4	BPH	BPH	BPH	BPH	BPH
5	Acinar adenocarcinoma, G.S.3+3,3+4, 4+4, 4+5	Adenocarcinoma, G.S. 4+3=7, PNI+	Adenocarcinoma, G.S-4+4=8	Adenocarcinoma G.S.4+3=7, G.G- 3	Acinar adenocarcinoma,G.S-3+3,3+4, 4+4, 4+5
6	BPH	BPH	BPH	BPH	BPH
7	B,C- Adenocarcinoma G.S.4+3=7 G.G. 3, D,A- Normal	Adenocarcinoma, G.S.-4+4=8 PNI +	Adenocarcinoma, G.S.-4+4=8 PNI+	B no Tumour, C Tumour G.G 1, G.S.-3+4+7	B,C- Adenocarcinoma G.S.-4+3=7, G.G- 3, D,A-Normal
8	G.S.- 4+3, 3+4,3+3,4+5,3+4	Adenocarcinoma, G.S.- 4+5 G.G.-5 PNI+	Adenocarcinoma, G.S.- 4+4=8 PNI+	Suspicious for malignancy, G.S.-3+4=7 , G.G.- 1	G.S.- 4+3, 3+4,3+3,4+5,3+4
9	A-E BPH, F- Adenocarcinoma No grade	BPH	BPH	BPH	A-E BPH, F- Adenocarcinoma No grade
10	BPH	Adenocarcinoma, G.S.- 3+3=6	BPH with focal suspicious	Adenocarcinoma, Urothelial carcinoma, G.S-5+4=9 ,G.G- 5	BPH
11	Adenocarcinoma, AC-G.S.-4+4=8 ,G.G.-4, B- 4+5=9, Gp 5	Adenocarcinoma G.S.- 4+4=8 No PNI	Adenocarcinoma G.S- 5+5=10, No PNI	BPH	Adenocarcinoma, AC G.S.--4+4=8 G.G.- 4,B- G.S.-4+5=9, G.G. 5
12	Inadequate for opinion	Inadequate for opinion	Inadequate for opinion	Inadequate for opinion	Inadequate for opinion
13	Adenocarcinoma, G.G- 5, G.S.-5+4=9, 80% tumour, No PNI	Adenocarcinoma , G.S.-4+5=9 80% tx, No PNI	Adenocarcinoma	5+5=10 Adenocarcinoma, TCC with glandular differentiation	Adenocarcinoma, G.G. 5, G.S.-5+4=9, 80% tumour, No PNI
14	adenocarcinoma, G.G.- 2, G.S.-3+4=7 PNI+ 50% Tx	Adenocarcinoma, G.G.-4+4=8 PNI+	Adenocarcinoma	Atrophy, BCH, Suspicious for malignancy	adenocarcinoma, G.G.- 2, G.S.-3+4=7 PNI+ 50% Tumour

Abbreviations G.G.- Group grade, G.S.- Gleason's score, BPH- Benign Prostatic hyperplasia, BCH- Basal cell hyperplasia, PNI- Perineural invasion, TCC- Transitional cell carcinoma.

Table 2: Interobserver and intraobserver correlations with their kappa and interpretation

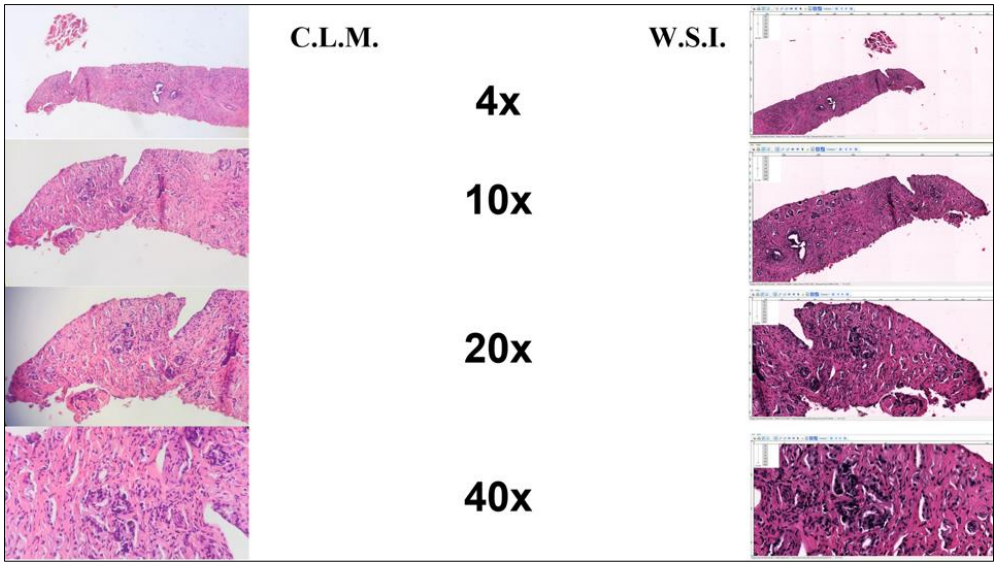
Agreement Type	Pathologists	Kappa Value	Standard Error (SE)	95% Confidence Interval (CI)	Interpretation
Interobserver (WSI)	Pathologist 1 vs 2	0.631258	0.33	-0.01531 to 1.0	Good agreement
Intraobserver (WSI vs CLM)	Pathologist 1	0.63415	0.32894	-0.01058 to 1.0	Good agreement
Intraobserver (WSI vs CLM)	Pathologist 2	0.6	0.24249	0.012473 to 1.0	Moderate agreement

The interobserver agreement between Pathologist 1 and Pathologist 2 for whole slide imaging (WSI) yielded a kappa value of 0.631 (SE = 0.33), with a 95% confidence interval (CI) ranging from -0.015 to 1.00. This kappa value indicates a "good" level of agreement, signifying strong concordance between the two pathologists in their WSI diagnoses.

Similarly, the intraobserver agreement for Pathologist 1 between WSI and conventional light microscopy (CLM) resulted in a kappa value of 0.634 (SE = 0.329), with a 95% CI ranging from -0.011 to 1.00. This score also falls within the "good" agreement range, demonstrating that Pathologist 1 maintained a consistent diagnostic performance across both WSI and CLM modalities.

Intraobserver Agreement: Pathologist 2 (WSI vs CLM) For Pathologist 2, the intraobserver agreement between WSI and CLM produced a kappa value of 0.600 (SE = 0.242), with a 95% CI spanning from 0.012 to 1.00. This result indicates "moderate" agreement, placing the score near the upper threshold of this category. Therefore, Pathologist 2 showed a moderate level of consistency in diagnoses between WSI and CLM.

DISCUSSION



Study found an intraobserver agreement for final diagnosis for cases, at Cohen's kappa of 0.63 and 0.60 in pathologist 1 and pathologist 2 respectively.

Table 3: Comparison of studies for WSI of prostate biopsies

Sr No	Study	No of cases	Intraobserver agreement among pathologists	Interobserver agreement
1	Helin et al, 2005 [9]	62	0.55 to 0.62	
2	Fine et al, 2007 [10]	30	0.586 to 0.819	
3	Kwast et al, 2010 [11]	20	0.21 to 0.39	
4	Rodriguez-Urrego et al, 2011 [12]	50	0.72	
5	Chargari et al, 2011 [13]	68	0.49	
6	Rao et al, 2021 [14]	70	0.90 to 0.96	-
7	Present study	14	0.60 to 0.63	0.63

CONCLUSION

The results indicate a high concordance in benign prostate lesion diagnoses but notable variability in adenocarcinoma grading, Gleason scores (G.S.), and perineural invasion (PNI) identification between the two pathologists by comparing WSI with conventional light microscopy (CLM), the study evaluates its accuracy, consistency, and diagnostic reliability. The findings indicate that WSI is comparable to CLM, making it a viable alternative for histopathological evaluation. With its high-resolution digital imaging, remote accessibility,

and potential for AI integration, WSI can be safely incorporated into routine clinical practice for prostate core biopsy diagnosis, improving workflow efficiency and diagnostic accessibility.

Technical limitations:

Several technical limitations were encountered during the Whole Slide Imaging (WSI) process. Some slides required rescanning due to initial focus issues, while one slide was mistakenly scanned upside down, leading to diagnostic discrepancies. The scanning system accommodates 15 slides per cassette, allowing for simultaneous scanning of 15 cases, with an average scan time ranging from 45 minutes to 1.2 hours. Scanning a total of 61 cases took approximately 4 to 5.2 hours.

Despite rescanning efforts, certain image areas remained unclear, likely due to tissue layering on the glass slides. However, these unclear regions accounted for less than 5% of the total WSI images and did not show a significant difference from those observed under conventional light microscopy (CLM). Additionally, technical artifacts such as dust, debris, and air bubbles in DPX-mounted slides were noted. These artifacts could not be entirely eliminated, posing further challenges to image quality.

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