RESEARCH ARTICLE

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Adequate Tissue Submission from Transurethral Resection Specimens for Detecting Incidental Prostate Carcinoma: Diagnostic Accuracy and Cassette Utilization in Thailand

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Abstract

Objective: To identify an adequate amount of prostate chip submissions with optimal diagnostic accuracy and minimal cassette utilization for the detection of incidental prostate carcinoma (IPC). **Methods:** We recruited consecutive transurethral resection specimens from patients with bladder outlet obstruction related to benign prostatic hyperplasia (BPH) and excluded patients with known or suspected prostatic carcinoma. Submission in the retrospective cohort depended on weight: either ≤12 g submitted entirely or >12 g submitted partially (initial 12 g with additional sampling). Submission was entire in the prospective cohort. The five different submissions (index test) were: initial 12 g, initial 12 g with additional cassettes per 10 g (12 g + q10 g), 12 g + q5 g, 20 g, and 20 g + q10 g. The diagnostic accuracy of the index test, compared to actual tissue submission (reference standard), was measured by the area under the receiver operating characteristic curve (AUC), with ≥95.0% considered acceptable. **Results:** A total of 451 patients (384 retrospective and 67 prospective) were included. The specimens had a median weight of 22 (range: 1-235) g, corresponding to a median cassette use of 10 (1-48) blocks, resulting in 5,010 total blocks. The average weight per block in the prospective cohort was 2 g. IPC detection rates were 6.3% retrospectively, 9.0% prospectively, and 6.7% overall. The first cassette containing carcinoma appeared between the 1st and 24th. Only three tissue submission strategies achieved acceptable diagnostic accuracy using lower estimated cassette numbers: 12 g + q5 g: AUC 98.3%, using 4,362 blocks, 20 g + q10 g: AUC 98.3%, using 4,239 blocks, 20 g: AUC 95.0%, using 3,373 blocks. **Conclusion:** Submitting 20 g of prostatic chips offers excellent diagnostic accuracy for IPC detection with reduced cassette utilization.

Keywords: Incidental prostate carcinoma- Transurethral resection- Tissue submission- Detection rate

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Introduction

Prostate cancer is the second most common cancer in men worldwide [1]. The incidence varies markedly by region, being highest in Northern Europe and lowest in South-Central Asia [2]. Incidental prostate carcinoma (IPC) is an adenocarcinoma that is unexpectedly detected after surgical treatment of benign prostatic hyperplasia (BPH). Most IPC cases are low risk, but high-grade cases require intervention. The detection rate of IPC was 10% in a meta-analysis [3], but only 4% in Thailand [4]. Different methods of tissue submission for pathologic evaluation also affect detection rates, with 8% from partial submission (initial 10 cassettes and additional cassettes per 10 g of the remaining tissue, 10 blocks + q10 g) compared to 19% from complete submission [5]. The virtual reduction of the cassette number to 10 cassettes resulted in 96% actual detection rate, missing one case of stage T1a/International Society of Urological Pathology (ISUP) grade 1. A cut-off of 10 cassettes resulted in a 43% reduction in cassette numbers [5]. The submission of 12 g of randomly selected prostatic chips detected almost 90% IPC, including all clinically significant neoplasms [6]. The College of American Pathologists (CAP) recommends submitting specimens weighing 12 g or less in their entirety, while submitting the initial 12 g and/or one additional cassette for every extra 5 g of remaining tissue (12 g + q5 g) [7, 8].

There is limited evidence regarding the optimal amount of tissue required to balance diagnostic accuracy and resource utilization in Thailand. However, these known submission guidelines may be excessive in number.

This study aimed to identify an adequate amount of prostate chip submissions with optimal diagnostic accuracy and minimal cassette utilization for detecting

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incidental prostate carcinoma.

Materials and Methods

Patient characteristics and study design

We recruited consecutive prostatic chip specimens (retrospectively from January 1, 2020, to October 31, 2023, and prospectively from November 1, 2023, to October 31, 2024) from the Pathology Laboratory of the Thammasat University Hospital. Transurethral resection, either transurethral resection of the prostate (TURP) or holmium laser enucleation of the prostate (HoLEP), was performed to treat bladder outlet obstruction related to BPH. Patients with known or suspected prostate carcinoma were excluded. We followed the patients with tissue submission less than 12 g + q5 g from the medical record.

Tissue submission

The actual tissue submissions in the retrospective cohort followed the CAP recommendations for specimens weighing 12 g or less as the entire submission. The gross examiner submitted specimens weighing > 12 g as partial sampling by submitting the initial 12 g (6–8 cassettes), and an additional cassette per 5 g of the remaining tissue may be submitted [7]. Partial submissions of prostatic chips were randomly selected. All tissues were submitted to the prospective cohort (complete submission).

The five index tissue submissions were 1) initial 12 g, 2) initial 12 g with an additional cassette per 10 g (12 g + q10 g), 3) 12 g + q5 g, 4) 20 g, and 5) 20 g + q10 g.

Histopathologic diagnosis

One pathologist (AS, AP, NA, and NW) reviewed the histological slides to establish a diagnosis of carcinoma according to WHO classification [9] or BPH. Clinical information and original diagnoses were not available to the reviewers. In the case of carcinoma, the reviewer recorded the histologic grade [10], tumor percentage [7] and the number of cassettes containing carcinoma. In complicated cases, additional immunohistochemical staining (34betaE12, p63, and Alpha methylacyl CoA racemase [AMACR]) and/or consensus between at least two pathologists were necessary to reach a final diagnosis. We categorized the histologic grade group (GG) in the ISUP as "low" when GG 1 to 3 and "high" when GG 4 or 5. The pathologists estimated the tumor quantity from histologic slides as a percentage and defined involvement of less than 5% as a low tumor percentage.

Statistical analysis

Baseline characteristics are presented as numbers and percentages for binary or categorical data and means with standard deviations or medians with ranges for continuous data. The association between variables was based on Fisher's exact test for binary or categorical data and the Wilcoxon rank-sum test for continuous data. The diagnostic measures of different tissue submissions (index test) were compared with the actual tissue submissions (reference standard) for IPC detection. Estimation of the average prostatic chip weight per cassette obtained from those weighing > 12 g in a prospective cohort.

The diagnostic accuracy metrics were the sensitivity, specificity, and area under the receiver operating characteristic curve (AUC). We determined the adequate amount based on an AUC reaching at least 95.0% and assessed the equality of AUCs using the chi-squared test. NW performed the statistical analysis using Stata IC 16.1 with a two-sided significance level of $p < 0.05$.

Study size estimation

Assuming pathologic evaluation of prostatic chips from transurethral resection as a diagnostic test to detect IPC with a sensitivity of 95%, prevalence of 5%, confidence interval of 9%, and confidence level of 95%, the estimated required sample size was no less than 451 specimens. Considering a possible 30% exclusion rate, the maximum number of eligible cases was 586.

Results

A total of 481 consecutive transurethral resection specimens were obtained from the prospective (n = 68) and retrospective cohorts (n = 413) and known or suspected prostatic carcinomas were excluded (n = 30) (Figure 1).

The eligible 451 cases (67 prospective and 384 retrospective) had a median age of 71 years (range: 46-92). The two cohorts had similar ages and prostate-specific antigen (PSA) levels. The retrospective group had a higher proportion of HoLEP (36% vs. 10%) and more prostatic chip weight (median 23 g vs. 13 g; > 12 g in 70% vs. 51%) (Table 1). Tissue submissions in the retrospective cohort were complete in 188 cases (49%), 12 g + q5 g in 186 cases (48%), and less than 12 g + q5 g in 10 cases (3%) (Tables 1 and 2). In the overall cohorts, IPC detection rate was 6.7% (30/451). Of these, 6.3% (24/384) were from the retrospective cohort and 9.0% (6/67) were from the prospective cohort. The IPC cases showed 80% (24/30) low-grade ISUP and 73% (22/30) low tumor quantity. The pathologic review did not change the ISUP grade and tumor quantity from the original diagnosis.

The average tissue weight per cassette was derived from prospective cases weighing >12 g (n = 34); a total weight of 1,177 g and a total cassette of 588 blocks; thus, the average weight per cassette was 2.0 g. The median first tumor-positive cassette in both cohorts was 1st (range 1st-24th) with 90th percentile detected at the 13th block; the retrospective cohort was 2nd (range 1st-24th), and the prospective cohort was 1st (range 1st-13th).

Ten retrospective cases from HoLEP had tissue submissions of less than 12 g + q5 g with specimen weights varying from 49 to 235 g, embedded in 8 to 30 blocks, and diagnosed with BPH. Upon follow-up, the patients were clinically well and showed no increase in PSA levels (Table 2).

If only 12 g or less were submitted, it would miss five IPCs that had the first cassette at 9 to 24 blocks, low tumor % (5% or less), GG1, and mostly low PSA levels (Table 3).

The five tissue submission protocols were 12 g, 12 g + q10 g, 12 g + q5 g, 20 g, and 20 g + q10 g. Only three protocols achieved the expected AUC without being statistically different from the actual submission; 12 g + q5 g, AUC 98.3% (p = 0.317); 20 g, 95.0% (p = 0.073);

Table 1. Baseline Characteristics (n = 451)

	All (n = 451, 100%)	Retrospective (n = 384, 85%)	Prospective (n = 67, 15%)	p-value
Age in years,				
Median (min-max)	71 (46-92)	70 (46-92)	71 (54-90)	0.292
<65	97 (22%)	82 (21%)	15 (22%)	0.872
≥65	354 (78%)	302 (79%)	52 (78%)	
PSA in ng/ml, n (%)	n = 363	n = 301	n = 62	
Median (min-max)	5 (0.4-92)	5 (0.4-92)	5 (0.4-68)	0.533
<10	273 (75%)	226 (75%)	47 (76%)	1
10-20	57 (16%)	47 (16%)	10 (16%)	
>20	33 (9%)	28 (9%)	5 (8%)	
Operation				
TURP	305 (68%)	245 (64%)	60 (90%)	<0.001
HoLEP	146 (32%)	139 (36%)	7 (10%)	
Specimen weight (g)				
Median (min-max)	22 (1-235)	23 (1-235)	13 (1-135)	<0.001
Min – 12 g	150 (33%)	117 (30%)	33 (49%)	0.005
>12 g	301 (67%)	267 (70%)	34 (51%)	
Tissue submission				
Complete	255 (57%)	188 (49%)	67 (100%)	<0.001
Initial 12 g + q5 g	186 (41%)	186 (48%)	.	
Initial 12 g + less than q5 g	10 (2%)	10 (3%)	.	
Cassette number				
Total	5,010	4,285	725	
Median (min-max)	10 (1-48)	10 (1-40)	9 (1-48)	0.27
IPC (detection rate)	30 (6.7%)	24 (6.3%)	6 (9.0%)	0.424
Tumor quantitation (%)				
Median (min-max)	1 (1-80)	1.5 (1-80)	1 (1-30)	0.479
pT1a as	22 (73%)	18 (75%)	4 (67%)	0.645
5%	8 (27%)	6 (25%)	2 (33%)	
pT1b as >5%				
Grade group				
1	18 (4.0%)	13 (3.5%)	5 (7.5%)	0.399
2	4 (0.9%)	4 (1.0%)		
3	2 (0.4%)	2 (0.5%)		
4	3 (0.7%)	3 (0.8%)		
5	3 (0.7%)	2 (0.5%)	1 (1.5%)	
Number of first cassette containing carcinoma Median (min-max)	1 (1-24)	2 (1-24)	1 (1-13)	0.598

HoLEP, holmium laser enucleation of the prostate; IPC, incidental prostate carcinoma; PSA, prostate-specific antigen; TURP, transurethral resection of the prostate.

and 20 g + q10 g, 98.3% (p = 0.317). The 20 g submission missed 3 cases (#182, #221, and #394), 12 g + q5 missed 1 case (#514), and 20 g + q10 missed 1 case (#182).

Considering cassette use and reduction from CAP submission, 20 g had the lowest block number at 3,373 blocks, 22.7% reduction while 20 g + q10 g used 4,239 blocks, 2.8% reduction (Table 4).

Processing one cassette requires approximately 10 minutes of technician time and costs about 40 Thai Baht (THB). A pathologist can evaluate a slide in 2 minutes. Compared with the CAP recommendation for tissue submission, the 20 g protocol yielded an estimated saving of 39,560 THB (134,920 vs. 174,480 THB), 165 technician hours, and 33 hours of pathologist review time, representing a substantial reduction in workload and cost without compromising diagnostic accuracy.

Discussion

Our IPC detection rates varied with the amount of tissue submitted: 6.3% in partial submission, 9.0% in entire submission, and 6.7% in both cohorts. The majority

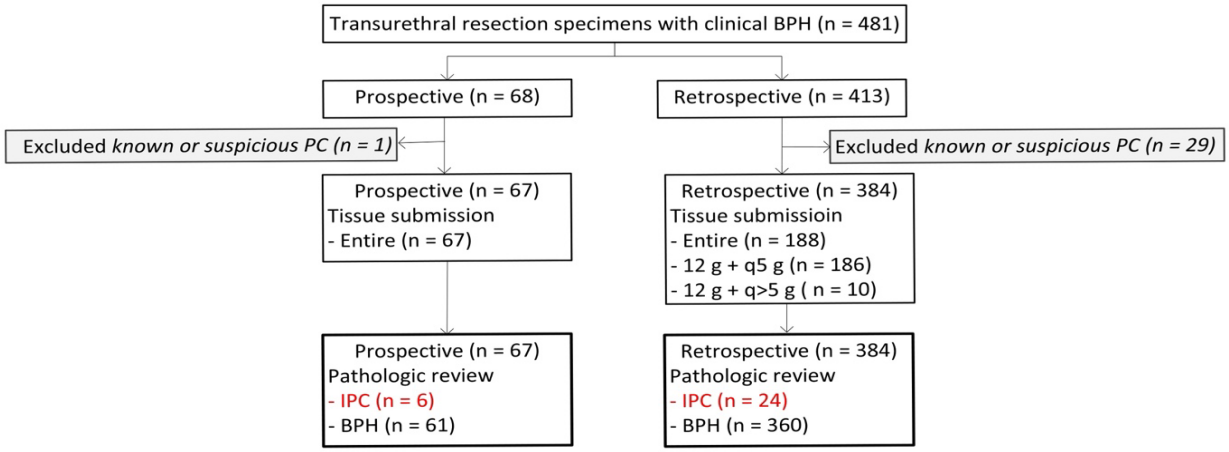

Figure 1. Flow of Participants

Table 2. Clinicopathologic Features of Specimen Sampling Less than 12 g + q5 g (n = 10)

Case	Age (years)	PSA (ng/ml)	Weight (g)	Block	FU (month)	FU findings
87	62	7	88	15	17	PSA = 0.8
88	79	4	58	12	39	well
153	70	17	72	8	40	PSA = 1
339	70	12	113	20	15	well
341	81	8.1	49	10	21	well
355	67	4	84	10	13	well
369	73	17	128	25	18	PSA = 1
371	66	10.2	235	30	14	PSA = 1
389	76	N/A	89	20	15	well
396	87	N/A	145	25	17	well

FU, follow-up; N/A, not available; PSA, prostate-specific antigen.

Table 3. Clinicopathologic features of 5 False Negative Cases if Embedded Less than 12 g.

Case	Age (yr)	PSA (ng/ml)	Weight (g)	Total block	First block with IPC	Tumor (%)	GG
#182	83	18	132	37	24	1	1
#221	65	9	163	30	24	1	1
#394	73	4	71	19	14	1	1
#401	74	6	87	20	9	1	1
#514	80	2	20	13	13	1	1

GG, histological grade group; IPC, incidental prostate carcinoma; PSA, prostate-specific antigen

of IPCs were in ISUP GG1, and the tumor quantity was less than 5%, likely in the very low to low-risk group of prostate cancer.

Among the three potential submission protocols, the 20 g submission achieved an AUC of 95.0% and the highest cassette reduction of 22.7%. The 20 g submission missed

Table 4. Accuracy of Different Submission of Cassette Number for Detection of Incidental Prostate Carcinoma

Measure	12 g + q5	12 g	12 g + q10	20 g	20 g + q10
Sensitivity (%)	96.7	83.3	83.3	90	96.7
Specificity (%)	100	100	100	100	100
AUC (%)	98.3	91.7	91.7	95	98.3
P-value (vs actual submission)	0.317	0.016	0.016	0.073	0.317
False negative	1	5	5	3	1
Expected submission (2 g/cassette)	4,362	2,277	3,399	3,373	4,239
Cassette reduction compared to CAP submission (%)	0	47.8	22	22.7	2.8

AUC, area under the receiver operating characteristic curve; CAP, The College of American Pathologists recommendation (12 g + q5 g estimated as 4,362 cassettes).

three cases of ISUP GG1 with a low tumor quantity (1%). Improving diagnostic accuracy by adding more 989 blocks to reach an AUC of 98.3% by 12 g + q5 g submission (4,362 blocks) or 1,637 blocks to reach an AUC of 100% by actual submission (5,010 blocks) was excessive on the laboratory workload for clinically very low-to low-risk prostate cancer.

The diagnostic accuracy and cassette reduction of 20 g (10 blocks) submission were similar to those of a large contemporary cohort study in Germany [5]. Our findings of AUCs with assessment of equality (chi-squared test), block reduction, and details of missed IPC of five submission protocols also support the data suggesting that the complete submission of TURP specimens may not be necessary. In cases of minimal tumor involvement (≤5%), neither additional partial nor complete sampling altered the initial Gleason score or pathological stage, confirming the diagnostic adequacy of limited sampling [11].

The limitations of this study were as follows: 1) the retrospective component may have introduced variability in sampling practices and 2) the lack of long-term clinical outcomes of patients. Further studies assessing appropriate submission to detect ISUP GG4 or 5 IPC, clinical outcomes, and cost-benefit analyses could help standardize tissue submission practices.

In Thai healthcare settings, pathology laboratories often face budgetary constraints, high specimen volumes, and a low incidence of prostate cancer. While the CAP recommendations are widely followed, they were primarily developed based on Western populations, and there is limited data validating their applicability to Asian populations.

The proposed 20 g (10 blocks) submission strategy demonstrated high diagnostic accuracy and efficiency in resource utilization. However, it should not be considered a universal replacement for the CAP recommendation of submission, as minor cases of IPC could be missed. Instead, this protocol provides a practical, evidence-based compromise for laboratories with budgetary limitations. The estimated reduction in cassette use (22.7%) corresponds to substantial time and material savings, underscoring the potential benefit in settings with high specimen volume and limited resources. Laboratories adopting this approach should ensure clinicopathologic correlation to minimize the risk of missed diagnoses.

In conclusion, the overall incidence of incidental prostate carcinoma in our study was 6.7%. Complete submission of TURP specimens allowed accurate detection and provided reference data for evaluating tissue submission strategies. Extensive tissue submission can increase the detection rate of incidental prostate carcinomas. The 20 g (10 blocks) submission protocol provides a cost-effective and diagnostically reliable approach for incidental prostate carcinoma detection, particularly in laboratories with limited resources. Although not intended to replace the CAP recommendation, it serves as a practical and evidence-supported alternative for institutions seeking to balance diagnostic accuracy with workload efficiency.

Author Contribution Statement

PC and NW contributed to the study concept and design and drafted the manuscript. Data acquisition was performed by PC, AS, AP, NA, MY, and DV. Data analysis and interpretation were carried out by PC and NW. AS and AP provided critical revision of the manuscript and supervision of the study. All authors have read and approved the final version of the manuscript.

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Data Availability Statement

The datasets generated and analyzed during the current study are not publicly available due to institutional and patient confidentiality policies but are available from the corresponding author on reasonable request.

Ethical Declaration

This research was conducted in accordance with the Declaration of Helsinki, and ethical approval was granted by the Human Research Ethics Committee of Thammasat University (Medicine) (No.MTU-EC-PA-0-146/66).

Conflict of Interest

The authors declare no conflicts of interest.

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