The association of level of practical experience in transrectal ultrasonography guided prostate biopsy with its diagnostic outcome

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ABSTRACT

INTRODUCTION The diagnostic yield of transrectal ultrasonography (TRUS) guided prostate biopsy is influenced by many patient and procedure specific factors. However, the role of operator specific factors remains inadequately defined. This study investigated the association of diagnostic outcome of TRUS guided biopsy with operator skill level.

METHODS This study looked at a consecutive cohort of 690 men undergoing their first extended pattern TRUS guided prostate biopsy by 27 operators over a 24-month period in a single institution. Logistic regression was used for statistical analysis.

RESULTS Biopsies performed by consultants (odds ratio [OR]: 2.35, $p=0.004$) and senior trainees (OR: 2.37, $p=0.002$) in patients with prostate specific antigen levels of $<10\text{ng/ml}$ were more likely to be positive than those performed by junior trainees (cancer detection rate 50.0%, 50.3% and 29.9% respectively). Furthermore, biopsies performed by junior trainees yielded a significantly higher proportion of prostate cancers with a Gleason score of $\geq 3+4$ than those performed by senior trainees (OR: 2.11, $p=0.031$) and consultants (OR: 2.40, $p=0.013$) (81.4%, 67.5% and 64.6% respectively). No significant differences emerged between operator skill groups for complications, rebiopsy rates or the number of prostate cancers found during the follow-up period (median: 34 months) of patients with a negative biopsy.

CONCLUSIONS Level of operator experience is associated with the diagnostic outcome of extended pattern TRUS guided biopsy. The findings of this study imply that case selection, self-audit and expert supervision for the duration of the learning curve should form the basis of biopsy training.

KEYWORDS

Biopsy – Prostate specific antigen – Operator effect – Transrectal ultrasonography – Prostate cancer

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Histological proof of malignancy is essential in the vast majority of prostate cancer cases. Transrectal ultrasonography (TRUS) guided biopsy was pioneered by Hodge¹ and is still regarded, in the extended pattern approach,² as an acceptable means of obtaining this histological information despite its limitations.⁵

It is estimated that in the UK alone, 89,000 such biopsies are carried out annually⁴ by operators with a variable level of experience and a diverse background, including urology, radiology and nursing.⁵ TRUS guided biopsy is a part of the urological curriculum, and yet neither the procedure itself nor the training and assessment are standardised. In fact, 68% of UK urology trainees involved in these biopsies believe they have not received enough training to perform the procedure.⁵

It is well established that the diagnostic yield of TRUS guided prostate biopsy is heavily influenced by a number of patient and procedure specific factors, including prostate

examination findings, serum prostate specific antigen (PSA) level, PSA density, presence of suspicious lesions on TRUS, and the number and direction of the biopsy cores. It is likely that the integration of these variables in an adequate patient specific biopsy strategy would depend heavily on operator skill level. However, this assumption has not been rigorously evaluated to date as TRUS guided biopsy is considered by many an easy procedure to learn. The purpose of this study was therefore to evaluate the association of diagnostic outcome in TRUS guided biopsy with operator skill level in a consecutive cohort of men undergoing their first such biopsy.

Methods

According to an electronic database at our institution, 842 TRUS guided prostate biopsies were performed between 1 August 2009 and 31 July 2011. These cases were screened

to exclude patients who had undergone previous prostate biopsies and/or those who had been diagnosed previously with prostate cancer. The final study cohort comprised 690 patients, none of whom had undergone prebiopsy magnetic resonance imaging of the prostate. A review was performed of electronic patient records, pathology results and audit records to establish the primary operator, serum PSA level, prostate volume on TRUS (calculated according to the ellipsoid volume equation [width × height × length × $\pi/6$]),

number of biopsy cores, histology result and complications (if any) for each patient in the cohort.

The biopsies were performed in an extended sextant pattern using a portable ultrasonography machine (SonoSite, Bothell, WA, US) with an end-fire transrectal probe and spring loaded biopsy needles (Bard, Tempe, AZ, US) on a pooled list under intravenous propofol sedation in a combination with periprostatic local anaesthetic block, as has been described previously.^{6,7} Triple antibiotic prophylaxis (a

Table 1 Descriptive analysis of patient characteristics, biopsy data and diagnostic outcomes

	Consultants	Senior trainees	Junior trainees
<i>Whole cohort</i>			
Number of patients	225	316	149
Median number of biopsies per operator	23.5 (IQR: 22)	19 (IQR: 31)	9 (IQR: 29)
Mean age (years)	68.9 (SD: 8.9)	68.3 (SD: 8.6)	67.8 (SD: 8.6)
Median serum PSA (ng/ml)	8.50 (IQR: 9.90)	8.45 (IQR: 8.25)	8.80 (IQR: 9.50)
Median TRUS prostate volume (cm ³)	46.00 (IQR: 35.00)	47.50 (IQR: 37.17)	40.00 (IQR: 32.00)
Median PSA density (ng/ml/cm ³)	0.18 (IQR: 0.14)	0.19 (IQR: 0.19)	0.19 (IQR: 0.27)
Median number of cores	12 (IQR: 0)	12 (IQR: 1)	12 (IQR: 1)
Cancer detection rate	64.0%	59.5%	47.0%
Median percentage of positive cores (%)	41.7 (IQR: 41.7)	40.0 (IQR: 46.7)	51.9 (IQR: 50.7)
Gleason $\geq 3+4$	64.6%	67.5%	81.4%
<i>Patients with PSA <10ng/ml</i>			
Number of patients	130	187	87
Mean age (years)	65.6 (SD: 7.7)	66.0 (SD: 7.9)	65.3 (SD: 7.7)
Median serum PSA (ng/ml)	6.10 (IQR: 2.30)	6.30 (IQR: 2.85)	6.70 (IQR: 2.90)
Median TRUS prostate volume (cm ³)	40.00 (IQR: 30.00)	44.00 (IQR: 34.00)	37.00 (IQR: 25.50)
Median PSA density (ng/ml/cm ³)	0.15 (IQR: 0.10)	0.13 (IQR: 0.11)	0.16 (IQR: 0.14)
Median number of cores	12 (IQR: 0)	12 (IQR: 0)	12 (IQR: 1)
Cancer detection rate	50.0%	50.3%	29.9%
Median percentage of positive cores (%)	33.3 (IQR: 33.3)	25.0 (IQR: 26.8)	33.3 (IQR: 50.0)
Gleason $\geq 3+4$	50.8%	51.1%	69.2%
<i>Patients with PSA ≥ 10ng/ml</i>			
Number of patients	95	129	62
Mean age (years)	73.3 (SD: 8.5)	71.6 (SD: 8.4)	69.7 (SD: 8.2)
Median serum PSA (ng/ml)	17.00 (IQR: 13.45)	20.40 (IQR: 19.70)	18.05 (IQR: 34.7[0])
Median TRUS prostate volume (cm ³)	55.00 (IQR: 40.00)	53.00 (IQR: 42.50)	46.50 (IQR: 49.25)
Median PSA density (ng/ml/cm ³)	0.27 (IQR: 0.36)	0.36 (IQR: 0.45)	0.42 (IQR: 1.09)
Median number of cores	12 (IQR: 0)	12 (IQR: 1)	12 (IQR: 1)
Cancer detection rate	83.2%	72.9%	71.0%
Median percentage of positive cores (%)	50.0 (IQR: 41.7)	50.0 (IQR: 50.0)	58.3 (IQR: 39.6)
Gleason $\geq 3+4$	75.9%	84.1%	88.6%

IQR = interquartile range; PSA = prostate specific antigen; SD = standard deviation; TRUS = transrectal ultrasonography

combination of oral ciprofloxacin, intravenous gentamicin and rectal metronidazole) was given.

The operators were grouped into consultants ($n=7$) and trainees ($n=20$). The trainees were further divided into a group of 9 junior and 11 senior trainees according to their experience in TRUS guided biopsies. All junior trainees started learning the biopsy skills during the study period. They were mentored by either a consultant or a senior trainee. The senior trainees had practised TRUS elsewhere for over a year and undertook biopsies independently during the study period.

Logistic regression (Stata® version 11, StataCorp, College Station, TX, US) was used for evaluation of the association between operator skill level and outcome of the biopsy (positive vs negative), Gleason score of found cancers (≤ 6 vs ≥ 7) and the proportion of positive cores ($<33\%$ vs $\geq 33\%$). Sub-group analysis was performed according to PSA level ($<10\text{ng/ml}$ vs $\geq 10\text{ng/ml}$). The learning curve was evaluated by applying a chi-squared test to pooled results of the first 15 and the last 15 TRUS guided biopsies undertaken by 4 junior trainees who had performed at least 30 such biopsies each.

The electronic records of patients who had a negative initial TRUS guided biopsy during the study period were

reviewed to establish how many had a subsequent prostate cancer diagnosis.

Results

Overall, cancer was found on biopsy in 402 of the 690 patients (58.2%). Among the 404 patients with serum PSA $<10\text{ng/ml}$, 185 were found to have cancer (45.8%) whereas among the 286 patients with PSA $\geq 10\text{ng/ml}$, cancer was detected in 217 (75.9%). The characteristics of the study cohort and the PSA subgroups are presented in Table 1 and Figure 1. Consultants, senior and junior trainees performed 32.6%, 45.8% and 21.6% of the total number of biopsies respectively, and similar proportions in each PSA stratified subgroup.

Association of operator skill level with cancer detection rate

Logistic regression analysis (Table 2) of the whole cohort indicates that biopsies performed by the consultants and senior trainees were more likely to be positive than those performed by junior trainees. When stratified by serum PSA value, the observed difference in the diagnostic outcome

Figure 1 Diagnostic outcomes of transrectal ultrasonography guided biopsies by operator group

Table 2 Association of operator experience with detection of prostate cancer on biopsy

	Whole cohort			PSA <10ng/ml			PSA ≥10ng/ml		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Junior vs senior trainees	1.66	1.12–2.45	0.012	2.37	1.38–4.07	0.002	1.10	0.56–2.15	0.784
Junior trainees vs consultants	2.01	1.32–3.06	0.001	2.35	1.32–4.16	0.004	2.02	0.94–4.35	0.073

CI = confidence interval; OR = odds ratio; PSA = prostate specific antigen

Table 3 Association of operator experience with detection of Gleason ≥3+4 cancer on positive biopsy

	Whole cohort			PSA <10ng/ml			PSA ≥10ng/ml		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Junior vs senior trainees	2.11	0.84–3.45	0.031	2.16	0.85–5.44	0.104	1.48	0.50–4.37	0.477
Junior trainees vs consultants	2.40	0.93–3.97	0.013	2.18	0.83–5.72	0.113	2.47	0.85–7.16	0.960

CI = confidence interval; OR = odds ratio; PSA = prostate specific antigen

remained significant in patients with PSA <10ng/ml while in the PSA ≥10ng/ml group, the difference was no longer significant although there was a trend towards a higher number of positive biopsies performed by consultants. No significant difference emerged in any patient group for the probability of a positive biopsy being performed by a consultant versus a senior trainee.

Association of operator skill level with yield of Gleason ≥3+4 cancers

Overall, biopsies performed by junior trainees yielded the highest proportion of Gleason ≥3+4 cancers. Logistic regression analysis (Table 3) indicated that junior trainees were much more likely to detect a Gleason ≥3+4 cancer on a positive biopsy than senior trainees or consultants. No difference in Gleason grading was observed between senior trainees and consultants. Furthermore, on stratification by serum PSA value, the difference in Gleason grading of positive biopsies was no longer significant between junior trainees and senior operator groups.

Learning curve of junior trainees

Pooled analysis of the first 15 and the last 15 cases of 4 junior trainees (who had performed at least 30 TRUS guided biopsies each) did not demonstrate a significant difference in cancer detection rates (CDR) or the median percentage of positive cores between the early and the later part of the learning curve.

Biopsy complications

Analysis of complications from electronic correspondence and weekly audit records showed an overall complication rate of 3.8% (26 recorded complications after 690 biopsies) with a broadly similar rate of complications among

consultants, senior and junior trainees (3.6%, 3.2% and 5.4% respectively).

Negative initial biopsies

The electronic records of the 288 patients who had a negative primary biopsy were reviewed at a median of 34 months after the procedure. These showed that 55 (19.1%) of these patients underwent a repeat biopsy during the follow-up period, with a median delay of 17 months. During the same time period, 24 patients (8.3%) with a negative initial biopsy were diagnosed with prostate cancer on either biopsy or transurethral resection of the prostate; 9 (3.1%) of these had high grade disease. When comparing data for junior trainees, senior trainees and consultants, there were no significant differences in rebiopsy rate or CDR during the follow-up period.

Discussion

The findings of our study substantiate the perception of urology trainees⁵ that the diagnostic outcome of TRUS guided biopsy is associated with the level of practical experience in this technique. Our data add to a small body of evidence regarding the association of operator experience with the outcome of such biopsies. Crucially, the majority of earlier studies compared the diagnostic outcomes in biopsies performed by operators of a similar level of experience, either senior versus senior⁸ or junior versus junior.^{9,10} The unique advantage of our study is the inclusion of operators across the whole spectrum of expertise and the follow-up of patients who had a negative initial biopsy.

As the analysis of baseline parameters of our cohort revealed a similar distribution of factors known to influence

the diagnostic yield of TRUS guided biopsy (PSA level, PSA density, patient age and number of cores), it is likely that the difference in CDRs between the operator groups is due to difference in technical ability to recognise the anatomy of the prostate, detect suspicious lesions on TRUS, design an individualised biopsy scheme and carry out biopsies in an efficient manner. Subtle changes in the biopsy technique (additional targeting of hypoechoic¹¹ and hyperechoic¹² lesions, lateral deviation of the biopsy needle² [aimed at oversampling of the tumour bearing peripheral zone and apex]) may significantly increase the diagnostic yield of primary TRUS guided biopsies. We hypothesise that such nuances in technique are essential for the diagnosis of low volume, non-palpable prostate cancer, which is typically characterised by serum PSA levels of <10ng/ml.

The lower diagnostic yield of biopsies performed by junior trainees in our study is in agreement with the results of Hori *et al*, who demonstrated a statistically significant decrease in the diagnostic yield of the first 50 TRUS guided biopsies in patients with serum PSA levels of <9.9ng/ml compared with experienced physician operators.¹⁵ In contrast, Henderson *et al* found no statistical difference in the diagnostic outcomes of 250 consecutive TRUS guided biopsies as performed by two consultants, two inexperienced nurse practitioners and a urology trainee with over a year's experience in such biopsies.¹⁴ However, CDRs in the latter study (44–45%) were below the diagnostic yield of biopsies even by junior trainees in our study (47.0%) and also below figures quoted by Hori *et al* (52.7–57.3%)¹⁵ despite a similar proportion of patients with PSA <10ng/ml in these cohorts (60%, 59% and 58% respectively).

The previous studies on TRUS guided biopsies that excluded the most (or the least) experienced operators showed a lack of a learning curve. A review by Benchikh El Fegoun *et al* of 770 patients biopsied by 24 residents over a 3-year period (with just over 30 biopsies per trainee) found no improvement in CDR between the first and the sixth month of training.¹⁰ Likewise, Karam *et al* retrospectively evaluated the records of 170 patients who underwent biopsy by an unreported number of residents, categorised into 4 groups according to the year of training, and concluded that there was no learning curve.⁹ However, their findings could be explained by the small size of the study cohort and only 5.5% of the biopsies were performed by the most experienced residents.

Lawrentschuk *et al* analysed the results of 4,724 primary TRUS guided biopsies performed by a group of very experienced operators.⁸ Although they could not demonstrate a learning curve, CDRs varied significantly from 43.8% to 52.4% among the individual operators, which the authors attributed to unknown differences in expertise or technique.

The lack of an obvious learning curve (as defined by improvement in CDR) among junior trainees in our study is not surprising. Only 4 trainees in the group performed more than 30 primary biopsies during the study period and none crossed the 50-case threshold recommended by Hori *et al*.¹⁵ On the other hand, our data demonstrate that the diagnostic performance of senior trainees is similar to that of consultants, implying that a learning curve does exist but that the

limitations of this study make precise definition of the learning curve difficult.

The predilection towards higher grade tumours in biopsies undertaken by junior trainees probably reflects the higher proportion of Gleason 6 cancers detected by the more experienced operators. Intuitively, a larger and/or multifocal tumour is easier to detect than a small and unifocal one, assuming a random biopsy sampling scheme with a set core density. Likewise, a tumour of any size is easier to detect in a small rather than a large prostate. Indeed, not only do tumours with a higher Gleason score tend to have a larger volume¹⁵ but higher grade tumours also tend to occur in smaller prostates,¹⁶ suggesting that they may be easier to diagnose by an inexperienced operator, leading to a higher proportion of Gleason ≥ 7 cancers among biopsies performed by junior trainees.

Study limitations

The retrospective nature of our study means that selection bias and undetected confounding factors may have influenced the outcomes. However, it is unlikely that significant selection bias was present given the uniform distribution of the established predictive risk factors for a positive biopsy among the patients in different groups.

Second, our practical definition of operator groups is largely an oversimplification, based on formal seniority and approximation of experience in TRUS guided biopsy rather than any specific indicator of proficiency. Considering that significant differences in TRUS guided biopsy outcomes exist even among very experienced operators,⁸ it is likely that these were present among the operators in our study.

Finally, as with many biopsy studies, our conclusions are likely to be affected by verification bias.¹⁷ This is because it is not possible to establish the true proportion of false negative biopsies performed by different operator groups.

Biopsy complications

Analysis of recorded complications in patients undergoing primary biopsies demonstrated that overall risk was low at 3.8% with 0.7% being hospitalised for sepsis. Our hospitalisation rate for postbiopsy sepsis compares favourably with figures reported in screening-based cohorts.^{18,19}

Negative initial biopsies

Taking into account the short follow-up duration in this study, our rebiopsy rate (19.1%) is typical for such cohorts. Medium-term follow-up studies suggest that 30–40% of patients undergo one or more repeat biopsies within five years of the primary negative TRUS guided biopsy.^{20,21}

It is estimated that initial TRUS guided biopsies miss up to 25% of cancers,^{22,25} some of which can be aggressive in nature.²⁴ In our cohort, only a few patients (3.1%) were diagnosed with Gleason $\geq 3+4$ cancer during the follow-up period, with no evidence of a worse diagnostic outcome for those who had undergone an initial biopsy performed by a junior trainee. Taken together with the fact that experienced operators found proportionally more Gleason 6 cancers at primary biopsy, these results suggest that many cancers missed by junior trainees were likely to be of low

grade and may therefore not have become apparent during the follow-up period.

Implications for training

Our results support the notion that increased experience in a given surgical procedure is associated with improved outcomes. There is a clear need for more consistent and standardised training in prostate biopsy techniques, as evidenced by trainee feedback,⁵ and the findings of this study and that by Hori *et al.*¹³ This need is made more acute by the fact that patients tend to experience more discomfort when biopsied by trainees.²⁵

Similar to any other surgical procedure, case selection should form an integral part of prostate biopsy training. Our data and those of Hori *et al.*¹³ suggest that trainees should focus their practice on patients with serum PSA levels of ≥ 10 ng/ml as diagnostic outcomes for initial extended pattern TRUS guided biopsies in this patient group are similar for novices and experienced operators. In the mixed patient cohort, a learning curve of more than 30 TRUS guided biopsies would be expected and in a low intensity training environment, it might even exceed the requirement of 50 cases suggested by Hori *et al.*¹³

Conclusions

Level of operator experience is associated with the diagnostic outcome of extended pattern TRUS guided biopsy. Experienced operators found more cancers in men with serum PSA < 10 ng/ml than the junior trainees. A larger proportion of cancers found by the least experienced operators had a Gleason score of ≥ 7 . There was no difference in rebiopsy rates and the number of cancers found during follow-up review of negative biopsies, implying that most cancers missed by junior trainees were likely to be low grade. The findings of this study indicate that case selection, self-audit and expert supervision for the duration of the learning curve should form the basis of TRUS guided biopsy training.

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