Upgrading of Standard and Transperineal Transrectal Ultrasound Guided Prostate Biopsies on Subsequent Radical Prostatectomy: A Population Based Study

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Citation

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Abstract

Gleason grade on prostate biopsy is a major component on which treatment decisions for prostate cancer are based. However a significant percentage, approximately 30% of patients with Gleason 6 disease who subsequently undergo radical prostatectomy are upgraded to Gleason 7 or higher.[1]

Correct grading of prostate cancer in the Gleason 6 population when compared to radical prostatectomy histology occurs in approximately 50-60% of cases.[3]
Grading inaccuracy on prostate biopsy is therefore of significant concern in patients who receive radiotherapy or active surveillance, as the true grade of their prostate cancer may never be determined and had they been upgraded they may not have opted for non-extirpative treatment.

This study therefore, utilises the population based SA-PCCOC (South Australian Prostate Cancer Outcome Collaborative) database to assess upgrading in Gleason 7 prostate cancer, as this group of patients are candidates for both surgical, radiotherapy and surveillance treatment options. (AUA guidelines for management of localised prostate cancer 2007, updated 2009)
A further analysis is performed to assess the upgrading rate for transperineal prostate biopsy (TP) as this technique has been suggested to be a means to improve grading accuracy in prostate cancer .[4]

BACKGROUND

Gleason grade on prostate biopsy is a major component on which treatment decisions for prostate cancer are based. However a significant percentage, approximately 30% of patients with Gleason 6 disease who subsequently undergo radical prostatectomy are upgraded to Gleason 7 or higher.[1]

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A further analysis is performed to assess the upgrading rate for transperineal prostate biopsy (TP) as this technique has been suggested to be a means to improve grading accuracy in prostate cancer .[4]

METHODS

The SA-PCCOC database was initiated in 1996 and is the largest population based, prospective prostate cancer database in the Southern Hemisphere. It contains more than 7500 patients and captures approximately 50% of all new prostate cancer diagnosis in South Australia, from both the

private and public sectors. Current accrual is approximately 1000 new patients every year.
An initial audit was performed in 2011 to assess the rate of upgrading in patients with Gleason 7 prostate cancer on standard TRUS biopsy (either 3+4 or 4+3), who subsequently had a radical prostatectomy.
A subsequent audit was performed in 2012 to assess the rate of upgrading in patients who underwent a TP biopsy (any Gleason grade) and subsequently had a radical prostatectomy.
Explanatory variables assessed for the two populations included: patient demographics, PSA, TRUS biopsy grade, total cores, total positive cores, histology and duration to radical prostatectomy.
A separate analysis was performed in the standard TRUS biopsy population to assess upgrading in 'low volume' Gleason 4 disease.
This was defined as patients who had only 1 core positive for Gleason 4 disease, or 2 cores positive for Gleason 4 disease if more than 10 cores were taken.

The primary outcome variable for both populations was upgrading which was defined as:
- Increase in Gleason grade from 3+4 to 4+3 or higher
- Any increase in total Gleason score
- Presence of tertiary pattern 5 disease

Statistical analysis was performed using StataCorp. 2005. Stata Statistical Software: Release 9. College Station, TX: StataCorp LP.
Ethics approval was obtained from Southern Adelaide Clinical Research Committee – Ethics approval numbers 099.11 and 202.12 respectively.

RESULTS

A total of 531 patients had Gleason 7 prostate cancer with subsequent radical prostatectomy.
Of the 531 patients identified, mean age was 62.9 yrs, ranging from 46.8-77.1yrs in Gleason grade 4+3 group, and 42.8-79.7 in the 3+4 grade. 379 patients had a TRUS biopsy Gleason grade of 3+4, with the rest, 152, having Gleason grade 4+3.
Mean PSA at diagnosis was 8.6ng/ml,with a range of 1.2-94ng/ml in Gleason grade 3+4, and 2.47-50.2ng/ml in 4+3 grade.

Table 1

Table 1 demonstrates the rate of upgrading in the Gleason 3+4 and 4+3 populations as well as the 'low volume' Gleason 4 subset

Grade	3+4	4+3	1 Core Gl4	2 Cores Gl4
Up	104 (27%)	23 (16%)	18 (20%)	12 (29%)
Down	41 (11%)	63 (41%)	13 (14%)	4 (10%)
Same	234 (62%)	66 (43%)	59 (66%)	25 (61%)
Total	379	152	90	41

Univariate and Multivariate analysis was performed to assess potential risk factors for upgrading of TRUS biopsy pathology on subsequent radical prostatectomy specimen.

Table 2

Univariate Analysis, Outcome Variable: Upgrading of TRUS biopsy result

Variable	Coefficient	P Value	95% CI
PSA at Diagnosis	0.014	0.682	-0.05 –> 0.081
Time interval between Biopsy and RP	-0.005	0.03	-0.01 -> -0.0005
Number of Cores positive for Gleason 4	0.07	0.196	-0.03 -> 0.18
Age	0.02	0.157	-0.01 -> 0.066
Percentage of Total Cores Positive for Gleason 4	0.007	0.274	-.005 -> .019
Percentage of Total Cores Positive for Gleason 3	-0.002	.720	-.016 -> .011

Figure 1

Histogram of Time between TRUS biopsy and Radical Prostatectomy

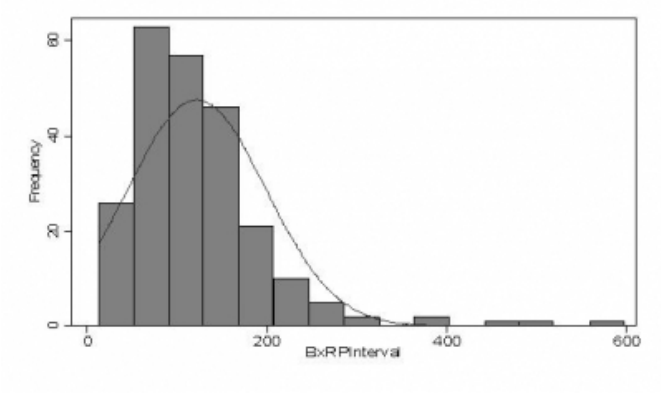


Table 3

Multivariate Analysis was performed utilising transformed and untransformed variable and a backwards building model.

Pseudo R2 = 0.0305

Variable	Coefficient	P Value	95% CI
Age	0.05	0.029	0.005 -> 0.1
Time interval between Biopsy and RP	-0.413	0.041	-0.81 -> -0.17

Mean age and PSA at time of biopsy were 64.6yrs and 12.7ng/ml respectively.

The indications for transperineal biopsy were:

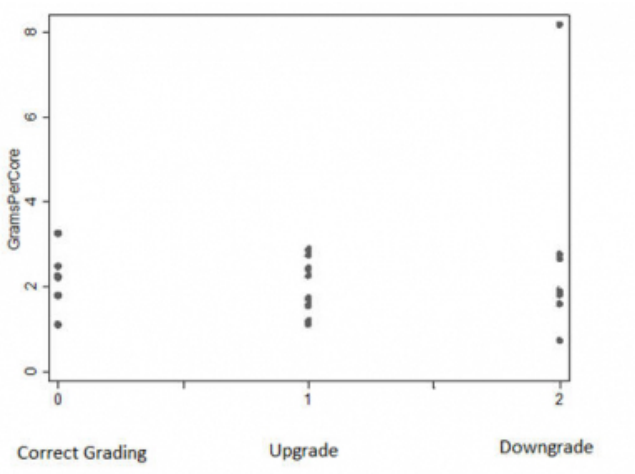
- Prior negative standard TRUS biopsy: 13 patients (56.5%)
- Prior positive standard TRUS biopsy: 8 patients (34.8%)
- Primary biopsy performed: 2 patients (8.7%)

The rate of upgrading in patients is illustrated:

- Upgrade on RP: 43.5% (10 patients)
- Downgrade on RP: 30.4% (7 patients)
- Stayed Same on RP: 26.1% (6 patients)

Figure 2

Prostate volume (as determined by RP weight) and number of cores was expressed as grams/core. The relationship between this and grading accuracy is illustrated below



DISCUSSION & CONCLUSION

The incidence of upgrading in prostate cancer in South Australia is not insignificant and in keeping with figures worldwide.

Multivariate analysis of upgrading in the Gleason 7 TRUS biopsy patients suggests that age and time between biopsy and RP is associated with upgrading. However it must be noted that the low R2 value of 0.03, indicates that future outcomes are likely to be poorly predicted by the model

Increasing age was found to be associated with an increased risk of upgrading. This is consistent with the ERSPC-Rotterdam trial, who also indicated that dedifferentiation occurs with increasing age.[5]

Increased time between biopsy and diagnosis was also associated with a decreased risk of upgrading. This is not biologically plausible, especially when compared to Active Surveillance series which suggest an increased risk in upgrading (increased rates of ECE, and worse pathology) in patients with significant delay in therapy. [5] South Australia appears to have only a small number of patients who have had transperineal biopsies and an even fewer number with subsequent radical prostatectomies. This likely indicates a variation in practice in between states in Australia. Only 26% of patients were accurately graded on TP biopsy with almost 50% being upgraded. Overall transperineal biopsy is not an accurate means of grading prostate cancer on its own, likely due its multifocal nature. The number of cores per gram of prostate tissue also does not appear to correlate with grading accuracy.

This suggests that the practice of using TP biopsy to reassess

prostate cancer prior to initiation of therapy such as active surveillance may not be an accurate reflection of the true grade of a patient's prostate cancer.

The significant incidence in upgrading on both standard TRUS and TP prostatic biopsy has implications for counselling of patients with prostate cancer especially when considering surveillance or non extirpative treatment options.

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