

Prostate cancer – other prognostic factors and reporting guidelines

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Prostate core biopsies

- Sextant biopsies (6 cores)
- Extended sextant (10-12 cores)
- Saturation/template biopsies (>20 cores)



Flat embedding

- Flat embedding should be employed in order to allow sectioning at multiple levels through the entire length of the core. This will maximise the amount of tissue for evaluation by the pathologist because cores can often become curved after fixation.
- Sponges can be used pre-embedding
- Metal tampers during embedding



Sectioning (core biopsies)

Prostate Cancer Risk Management Programme 2006

- When sectioning the cores, the laboratory should ensure that the cores have been optimally sectioned in order to identify even small foci of cancer. As a minimum, the laboratory should take sections at three separate levels of the core. Level 1 should lie in the top half of the core, level 2 in the middle and level 3 in the bottom half of the core.
- Spare sections at each level should be prepared at the initial time of sectioning because this will reduce the chance that the patient may need to be re-biopsied. As a minimum, four sections should be prepared at each level, one for haematoxylin and eosin (H&E) stain, two for immunohistochemistry and one as a spare.
- Only one section need be stained and examined at each level.
- Further sections at shallow levels should be performed if the pathologist finds something suspicious at a particular level.
[slide courtesy of Dr D Griffiths, Cardiff]



Terminology

When reporting prostate biopsies, ambiguous terms should be avoided. The following standard nomenclature should be used:

- benign
 - +/- acute inflammation
 - +/- chronic granulomatous inflammation
 - +/- atrophy
- high grade prostatic intraepithelial neoplasm (PIN or HGPIN)
- suspicious (lesion too small or insufficient criteria present): an indication for rebiopsy
- Adenocarcinoma (state tumour type e.g. prostatic acinar adenocarcinoma and Gleason e.g. as 3+3=6)



Extent of tumour in prostate core biopsies

There is no general agreement on how it should be reported. Data may include:

- *Number of cores involved (per separate specimen pot)**
- Linear length of tumour in all cores
- *Percentage of tumour in most involved core**
- *Total percentage of tumour in all cores (per separate specimen pot)**
- All the above but of "high grade" tumour rather than all tumour.

**this is what I do*

Minimum requirement: Number of cores involved, laterality (left versus right); some consistent indication of extent of tumour.



Does the extent of carcinoma in prostatic biopsies predict prostate-specific antigen recurrence? A systematic review.

Hamden P et al. *Eur Urol.* 2008;54:728-39

- Thirteen papers reporting on at least 100 patients were identified and included patients treated by watchful waiting or hormonal therapy (n=1), radical prostatectomy (n=11), or radiotherapy (n=1).
- Only two studies reported on clinical progression or mortality.
- The percentage of cancer in biopsies (overall percentage or the greatest percentage in the most involved core) was an independent predictor of prostate-specific antigen (PSA) and clinical outcomes regardless of the form of treatment and was generally superior to simply counting the number of positive cores
- The marked variability in study design, conduct, and reporting precluded meta-analysis of the data and precise risk estimation.



Active surveillance program for prostate cancer: an update of the Johns Hopkins experience. Tosoian JJ et al. *J Clin Oncol.* 2011;29:2185-90

Enrollment criteria for 'very low risk cancers':

- Clinical stage T1c
- PSA density less than 0.15ng/mL
- Gleason score 6 or less
- Two or fewer cores with cancer
- 50% or less cancer involvement of any core

Programme aimed mainly at older men

- 6 monthly PSA and annual 12-14 core biopsies performed

[Overall 33% of 255 men underwent intervention at a median of 2.2 years after diagnosis]



Active surveillance program for prostate cancer: an update of the Johns Hopkins experience. Tosoian JJ et al. *J Clin Oncol.* 2011;29:2185-90

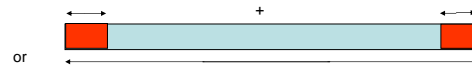
Conclusion:


- "Active surveillance with curative intent appears to be a reasonable alternative to immediate intervention for carefully selected older men"
- "Limiting surveillance to the lowest risk category of disease may reduce the incidence of adverse outcomes"
- "Nonetheless patients considering surveillance should be counselled on the possibility that delayed intervention may compromise the opportunity for cure in some cases"



Cancer estimate in biopsies

- One method <50% involvement; the other discontinuous involvement of 100%
- So criteria depends on methodology



 = cancer in above diagram

Pathological Outcomes in Men with Low Risk and Very Low Risk Prostate Cancer: Implications on the Practice of Active Surveillance Tosoian JJ et al. *J Urol.* [2013 in press]

- 7,486 subjects eligible for active surveillance who underwent radical retropubic prostatectomy were studied
- 153 met the criteria for 'very low risk', defined in the previous study
- Remaining 7,333 were 'low risk' (T1c or T2a, PSA less than 10, Gleason score 6 or less)
- For very low risk cases, Gleason score 7 or greater found in 13% cases; extraprostatic extension found in 8.5% cases



Perineural invasion

Not clear if this is strictly an independent prognostic indicator and what is PNI: i.e. limited to large nerves outside the tumour bulk or any nerves including those embedded in the tumour.



Invasion of fat

- Generally taken to be indicative of at least T3 disease (including if seen in a core biopsy)
- [NB Invasion of skeletal muscle is not necessarily indicative of extraprostatic extension, even in a prostatectomy – may be blending of skeletal muscle fibres with the prostate gland at the apex and sometimes anteriorly]



Vascular invasion

Very uncommon in biopsies; noted if present



Seminal vesicle in core biopsies

- If seminal vesicle type mucosa is seen in core biopsies of prostate that were not specifically targeted at the seminal vesicle, bear in mind that the lining of seminal vesicle and ejaculatory duct is similar and tumour involvement does not necessarily mean pT3b disease
- If tumour involvement present in wall of structures targeted clinically as seminal vesicle biopsies, pT3b can be suggested



Incidence and clinicopathological characteristics of intraductal carcinoma detected in prostate biopsies: a prospective cohort study

Watts K et al. *Histopathology* 2013;63:574-579



Quality control

Prostate Cancer Risk Management Programme 2006

The following information should be recorded and audited:

- the time from when the biopsy is taken to the time when the histology result is available to the clinical team
- the time from when the biopsy is taken to the time when the histology result is communicated to the patient
- the time from when the biopsy is requested to the time when the histology result is communicated to the patient
- the prevalence of prostate cancer among patients undergoing prostate biopsies
- the median number of biopsies performed per patient
- cancer rates within specified PSA ranges
- the sensitivity and specificity of initial biopsies for prostate cancer
- patient satisfaction with the procedure
- the incidence of urinary retention after biopsy
- the incidence of serious rectal bleeding
- the number of patients and reasons for admission for all patients requiring hospital admission within seven days of the biopsy
- the percentage of cores that contain prostatic tissue; the minimum percentage of cores found to contain prostatic tissue should be 95%
- the percentage of biopsies reported as 'suspicious'; this may reflect a number of factors, including the quality of the specimen, the population served and the certainty of the pathologists' reporting, but would not be expected to be more than 10%.



[slide courtesy of Dr D Griffiths, Cardiff]

TURPs

- For specimens <12 g, submit all tissue
- If >12g, submit 12 g (usually 6 cassettes) + 1 cassette for each additional 5 g (select chips that are firm, yellow or grossly suspicious for cancer)



Megablocks or standard blocks?



Extraprostatic extension: assessment of extent

- Epstein criteria:
 - Focal: a few neoplastic glands outside the prostate (82% progression free rate)
 - Established: anything more than focal (65% progression free rate)
- Wheeler criteria:
 - Focal: cancer extending less than 1 high power field outside the prostate in no more than 2 separate sections (73% 5 yr progression free rate)
 - Established: anything more than focal (42% progression free rate)



Prognostic significance of histopathological features of extraprostatic extension of prostate cancer

Danneman D et al. *Histopathology* 2013;63:580-589

- Radial distance of extraprostatic extension (EPE) beyond the prostate predicted recurrence after radical prostatectomy
- Number of foci of EPE, site, circumferential extent or perineural invasion at site of EPE did not predict recurrence
- 1.1mm (diameter of a x20 field) was optimum predictive cutoff in this study, though remains to be validated



Prostate cancer- TNM/AJCC classification, 7th edition, 2009

- T1 = Clinically inapparent tumour, not palpable or visible by imaging
 - T1a Tumour incidental histological finding in 5% or less of tissue resected
 - T1b Tumour incidental histological finding in more than 5% tissue resected
 - T1c Tumour identified by needle biopsy, e.g. because of elevated PSA
 - pT2 Tumour confined within the prostate
 - T2a Tumour involves one half of one lobe or less
 - T2b Tumour involves more than half of one lobe, but not both lobes
 - T2c Tumour involves both lobes
 - pT3 Tumour extends through the prostatic capsule
 - T3a Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
 - T3b Tumour invades seminal vesicle(s)
 - pT4 Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles and/or pelvic wall
- Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2
- There is no pT1 category because there is insufficient tissue to assess the highest pT category
- [*underlined text indicate change from previous 6th edition TNM where microscopic bladder neck invasion was previously classified as pT4]



Radical prostatectomy – assessment of tumour

- Location and amount of tumour
- Gleason
- Whether confined to prostate (pT2) or extraprostatic extension (pT3 or greater)
- Location and extent of extraprostatic extension
- Presence/absence and extent of margin involvement and its location (s)/extent
- Presence/absence of seminal vesicle invasion (pT3b)
- Presence/absence of perineural invasion
- Presence/absence of lymph node metastases/number of nodes involved/total lymph node count

