The Royal College of Pathologists
Pathology: the science behind the cure

Standards and Datasets for Reporting Cancers

Dataset for histopathology reports for prostatic carcinoma (2nd edition)

October 2009

Unique document number	G084
Document name	Dataset for histopathology reports for prostatic carcinoma
Version number	2
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Date active	October 2009
Date for review	October 2012
Comments	In accordance with the College's pre-publications policy, this document was put on The Royal College of Pathologists' website for consultation from 25 November to 23 December 2008. 24 pieces of feedback were received and the authors considered them and amended the document accordingly. Please email publications@rcpath.org if you wish to see the responses and comments. This version replaces the 1st edition of the dataset, published in 2001. Professor Carrock Sewell Director of Communications

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1. Introduction

In 2002, the National Institute for Health and Clinical Excellence (NICE) guidance, *Improving Outcomes in Urological Cancer* (www.nice.org.uk) recommended the establishment of specialist multidisciplinary teams for radical pelvic surgery (prostatectomies and cystectomies), serving a catchment population of one million. It was estimated that such a population would produce well in excess of the 50 surgical procedures (combined total) per annum, regarded as a minimum to maintain specialist expertise and allow audit of outcomes. Patients with prostate cancer diagnosed by local urological multidisciplinary cancer teams should be referred to the specialist team and the diagnostic slides made available for review. It is expected that pathologists reporting prostatic tumours participate in the NHS Prostatic Pathology External Quality Assessment (EQA) Scheme (details on www.rcpath.org/index.asp?PageID=1053), as recommended in the *Improving Outcomes* guidance.

The diagnosis of prostate cancer is now generally made on transrectal ultrasound (TRUS) guided prostatic biopsies, and it has been estimated that between 56 000 and 89 000 needle biopsies are performed per annum in England and Wales, equivalent to 1 million cores needing histological assessment. Biopsy procedures have varied widely both in terms of needle placement and numbers of cores taken, leading in 2006 to the publication of national guidance in an effort to standardise practice.[2] National guidance has attempted to check the inexorable rise in the number of men biopsied by recommending that a raised prostate specific antigen (PSA) alone should not be an absolute indication to proceed to biopsy,[3] but whether this will change ingrained practice is uncertain.

There are well-recognised difficulties surrounding the issue of prostatic cancer diagnosis and treatment, which prompted the development of a disease specific guidance, published by NICE in February 2008.[4] Most of the recommendations within the guidance are evidence based or represent best clinical practice, but a small number of recommendations have raised concern.[5] There were no pathologists on the Guidance Development Group, and this absence is reflected in the recommendations that incorporate pathological factors. The main areas of debate surround the review of patients with negative biopsies and the pathological criteria used to define low risk disease. In the first case, the Guidance Development Group stated that histological review of negative biopsies was not the routine intent of the Group,[4] but did not define the subset of patients for whom pathological review would be justified, so that practices are likely to vary with consequent difficulties in workforce planning, and continuing controversies for best practice in multidisciplinary team working. In terms of defining risk, the additional pathological criteria for low risk in patients with clinical stage T1c, low PSA density values and Gleason score 3+3=6, that is cancer in less than 50% of the total number of biopsy cores and less than 10 mm of any core involved, are not evidence based. Also, the guidance recommends that active surveillance should be the treatment of choice in these patients but that repeat biopsies, again increasing pathologists' workload, should be performed to exclude sampling error or progression, defined as a higher Gleason score or more extensive disease. This is because active surveillance, unlike watchful waiting where treatment is symptomatic, is based on the premise that radical intervention with curative intent is instituted if there are signs of progression.

The NICE guidance and the systematic evidence reviews undertaken in the preparation of this dataset have highlighted the considerable gaps in the existing evidence, and the consequent difficulties in counselling patients effectively. The development of a framework, whether within collaboratives or networks, to collect and validate additional data prospectively, is strongly recommended. These additional data items are included in this dataset.

Systematic evidence reviews have been performed in areas of controversy, particularly in the reporting of prognostic factors in prostatic biopsies. Elsewhere, the recommendations are based on best practice.

Guidelines for the reporting of prostatic tumour specimens are required and should be adopted for the following reasons:

- grading and staging of prostate tumours determine subsequent clinical management and follow-up
- consistent reporting of pathological risk factors will allow patients to make informed decisions about their care
- adoption of a consistent approach to risk assessment of prostatic cancers is essential for audit and epidemiological studies.

The consultation process (in progress) includes circulation to:

- British Association of Urological Surgeons (BAUS)/BAUS section of oncology
- British Uro-oncology Group
- National Cancer Research Institute (NCRI) Prostate Clinical Studies Group
- Prostate Cancer Risk Management Group
- Prostate Cancer Advisory Group
- The Royal College of Radiologists.

2. Clinical information required on the specimen request form

This includes the presenting PSA, the clinical context and the type of specimen, whether biopsy, transurethral resection, radical prostatectomy (nerve sparing or not) or nodal dissection. The number and site (at least laterality) of prostatic biopsies is important. Information about prior biopsies or resections, or prior treatment, helps in the interpretation of the microscopic findings within the appropriate clinical context. Anti-androgen therapy alters the cytology and architecture of both benign and malignant glands,[6,7] and may therefore alter the significance of Gleason grading. The date of completion of radiotherapy is also important as, even if therapy is effective, tumour can persist for at least two years after external beam radiation and for up to six years for brachytherapy.[8] Assessment of radiation effect is predictive of local failure.[9]

3. Preparation of specimens before dissection

3.1. Transurethral resections and enucleations

Resections received as prostatic ‘chips’ do not require sectioning prior to fixation. Enucleations or prostatectomies are generally restricted to large prostates in patients with lower urinary obstructive symptoms. Such specimens can benefit from a few incisions to allow formalin penetration. Inking of margins is not useful, even if carcinoma is detected incidentally, because these are not radical resections and, given the multifocality of prostatic cancer, demonstration of negative margins does not necessarily equate with absence of residual disease.

3.2. Radical prostatectomies

The prostate gland is covered by a very thin rim of connective tissue, which can easily be disrupted during surgery or in the pathology suite leading to ‘false positive’ margins. Distinction between true and false surgical margins is easier when the specimen is fresh, because fixation changes the colour and appearance of the gland. In the fresh state, at the apex, intact Denonvillier’s fascia should be identifiable posteriorly by its smooth, glistening surface. Surgical dissection of the fascia normally causes it to retract up over a short distance exposing underlying tissues, and this area should not be regarded as a true

surgical margin. A very small ring of sphincter muscle fibres is seen around the urethra. A small layer of connective tissue should also be present at the posterolateral edge to indicate the absence of capsular incision.[10]

Any surgical incision will expose underlying prostatic tissue, which is duller and more irregular than the covering fascia. Even small inadvertent incisions during the separation of the planes of dissection can result in relatively large areas of exposed glandular tissue if the prostate is under tension from hyperplasia and subsequently 'herniates' through the incision. An additional problem is the presence of clips or tight sutures required for haemostasis. The sutures in particular are easier to remove in the fresh state and are very difficult to identify if the specimen has been inked. For all of these reasons, surgeons in some European centres remove clips and sutures in theatre, and ink the true surgical margins themselves.

The specimen is fixed in an adequate volume of formalin. Injection of formalin into the specimen can help fixation and does not appear to affect tissue shrinkage and therefore tumour volume measurements.[11]

3.3. Lymphadenectomies

These are generally fixed *en bloc* in adequate volumes of formalin.

4. Specimen handling and block selection

Synoptic reporting proformas have been added as an *aide memoire* for the main features of these neoplasms (Appendices C–E). The proforma extracts the dataset currently used in diagnosis and staging for the most common situations, i.e. the incidental finding of carcinoma in transurethral resections (Appendix C), radical prostatectomy specimens (Appendix D) and prostatic biopsies (Appendix E) in patients with no previous history of treatment. These would usually be supplemented by a more detailed written report.

4.1. Gross examination

4.1.1. Transurethral resection of prostate (TURP)

The chips are weighed. In general, gross examination of chips for evidence of tumour, such as necrosis or induration, is unrewarding.

4.1.2. Enucleation specimens

Retropubic enucleations are generally reserved for large hyperplastic prostates. The specimen is weighed and measured in three dimensions. Sections often reveal nodular areas.

4.1.3. Radical prostatectomy specimens

Because of distortion due to hyperplasia in particular, the prostate can be difficult to orientate and identification of several landmarks is helpful. The posterior aspect is flatter than the anterior surface and has a midline groove. The seminal vesicles arise from this aspect, but are not necessarily removed *en bloc* (or at all), particularly during robotic surgery as excessive tension during dissection can shear the vesicles off the base of the prostate. The anterior surface is convex and shorter than the posterior. The base of the prostate (bladder neck) is flatter than the apex, which generally tapers to a more conical shape.

If the specimen has not been prepared in theatre or received fresh, following removal of the clips and sutures, it should be examined as described in Section 3.2 and inked accordingly. The use of different colours to identify laterality is an advantage. These can usually be superimposed on India ink if required. The specimen is weighed and measured in three dimensions.

The vas resection margins are sampled and the seminal vesicles amputated close to the prostate base. The first section from the apex is perpendicular to the urethra. Precise depth will depend on the shape of the apex but is generally 6–7 mm thick and angled so that the prostate will be in the correct anatomical position when laid on the cutting board. The posterior aspect usually has to be thicker than the anterior to achieve this. This section is then coned to demonstrate the relationship between any potential tumour and the peripheral margins. Sections should be taken with the overall aim of demonstrating the margin as extensively as possible. So-called 'shave' resection margins are discouraged as the presence of tumour simply indicates that tumour is close to, but not necessarily at, the inked resection margin.

Holding the remaining specimen as close as possible to the correct anatomical position, the prostate is then sliced into 4 mm sections, perpendicular to the urethra, using a Perspex board with 4 mm edges or other guide. Thinner sections may require the insertion of a foam pad or other device to prevent the section from curling during processing. The use of a silicone antislip mat can be useful to avoid movement of the board and specimen. It is important to avoid applying too much pressure to the specimen or the sections will be too thick. Also, sections should be taken with a smooth sweep of the knife (rather than sawing backwards and forwards) to give a flat surface for embedding. If the knife deviates when slicing so that a particular margin is not represented, it is useful to make a note of this to avoid an unnecessary request for levels. Sections are laid out sequentially so that each face is also embedded sequentially. Prostatic adenocarcinomas are visible macroscopically in just over half of the cases and an identifiable gross lesion is correlated with increased tumour stage, grade and size.[12]

It is useful to section the last slice of the base perpendicular to the initial, horizontal plane of excision. This demonstrates the margins more effectively and the distinction between the specialised smooth muscle of the prostate and detrusor muscle bundles is easier to appreciate, which is useful to assess potential tumour spread.

4.1.4. Lymphadenectomy specimens

Specimens are measured in three dimensions. Lymph nodes are identified and described as either macroscopically normal or involved by tumour. However, the correlation between nodal size and the presence of metastasis is poor in the prostate, with one study demonstrating that the mean longitudinal length of negative nodes was 35 mm (range 5–90 mm) compared with the smaller value of 16 mm (range 2–65 mm) for positive nodes.[13] These are often impalpable.

4.2. Block selection

4.2.1. Transurethral resection specimens and enucleations for clinically benign disease

A proportion of these specimens will contain unsuspected foci of carcinoma, and the optimum sampling strategy is controversial. The TNM classification distinguishes between cases with over 5% of resected tissue involved (pT1b) and those with smaller amounts of cancer (pT1a). The interpretation of this by pathologists has varied. Many, including the authors, assess the percentage of chips involved whereas others report the percentage of surface area involved. The latter is more difficult to report consistently particularly in large resections, and the percentage of chips involved provides valuable information (Berney et al, in press).

Up to 32% of patients with pT1b disease suffer clinical progression after four years,[14] whereas disease progression is slower for patients with pT1a disease, with up to 16% progressing at eight years.[14-16] Ideally, sampling protocols should identify all pT1b patients and pT1a patients with a life expectancy of eight years or more. A common protocol is to embed the entire specimen up to 12 g (six blocks) and a further 2 g (one block) for every additional 5 g. Although these additional blocks may detect a higher proportion of tumours,

they do not lead to upstaging or upgrading of pT1a tumours if tumour was present in the first six blocks.[17] Examination of the entire specimen is justifiable for the small subset of patients who may benefit from radical treatment on the basis of life expectancy. There are no data on optimum block selection in enucleation specimens, and the most consistent approach is generally to sample according to weight as for transurethral resections.

4.2.2. Transurethral resection specimens in patients with known prostate cancer

These resections are generally small and embedded in their entirety to detect residual cancer and assess response to therapy.

4.2.3. Radical prostatectomy specimens

Protocols based on series of less than 100 patients have detailed sampling strategies to detect the majority of prostatic tumours[18] and identify adverse pathological factors.[19] Nevertheless, complete embedding of the specimen, including seminal vesicles, is preferable for the following reasons:

- a high proportion of prostate cancers is not visible macroscopically and sampling would therefore be blind[12]
- in a large study of 1383 patients, those with negative margins using step sectioning of the entire specimen had a lower risk of progression than similar patients whose specimens were partially sampled[20]
- although the location of positive margins is not relevant to immediate patient management, surgical margin status is one of the tools used to audit the quality of surgery.

A further debate surrounds the use of large block technology versus small blocks for the consecutive sections of prostate. The use of large blocks is generally more cost effective, particularly when interpretative time is included. Assessment of extraprostatic extension (EPE), i.e. extension beyond the contours of the gland, and margin positivity are greatly facilitated. Potential drawbacks include the additional fixation and processing required, which may alter the immunoreactivity of the tissues. However, immunocytochemistry is rarely required in routine practice.

The specimen is dissected as described and sequentially embedded to identify:

- right and left vasa
- right and left seminal vesicles
- the coned apex with details of laterality and whether anterior or posterior
- consecutive sections of the prostate
- sections from the base with details of laterality and whether anterior or posterior.

4.2.4. Lymphadenectomy specimens

Palpable nodes are embedded individually. Processing of remaining fat often reveals small impalpable lymph nodes, which are more often the site of metastatic disease than the larger nodes.[13] The fat should be serially sliced at 2-4mm intervals and all embedded.

5. Core data items

Although the presence of rare variants should be recorded, the vast majority of prostatic carcinomas are of the microacinar variety. The critical parameters to record in a pathology report are the Gleason score, certain aspects of the pathological stage, including EPE (stage pT3a) and seminal vesicle invasion (stage pT3b) and margin status. The use of adjuvant treatments, including radiotherapy and hormone therapy, can be based on these variables. In addition, they can be used in mathematical models such as the Kattan nomogram[21] to predict the likelihood of recurrence in a given patient. The results of a review, for instance in the context of a multidisciplinary team discussion, will replace those

submitted by the original pathologist to the Cancer Registry, and it is helpful to Registry staff if it is clear whether the dataset is a primary submission or the result of a review.

5.1. Gleason grading

Although modifications to the Gleason grading system have been proposed for biopsy specimens, the current proposal by the International Society of Urological Pathologists[22] is to continue using the most prevalent and second most common grades to assign the Gleason sum score to radical prostatectomy specimens, and to mention the presence of a tertiary grade. A change to the grading of radical prostatectomy specimens has not been proposed because, although the incidence of seminal vesicle invasion and lymph node metastases was higher in patients with Gleason 4+3 plus a tertiary pattern than in those with Gleason 4+3 without a tertiary grade, it was not as high as in those with Gleason 4+5[23] in the limited data considered. However, a systematic evidence review demonstrated that patients with a tertiary grade, regardless of whether it was higher or lower than the primary and secondary grades, are at higher risk of biochemical relapse following radical prostatectomy.[24] Of the two papers subsequently published, one was a large study of 509 patients examined the significance of a tertiary pattern 5 in Gleason 7 prostate cancer.[25] When all cases of Gleason 7 prostate cancer with a tertiary grade 5 were compared with all those without a tertiary grade 5, the presence of a tertiary grade 5 was associated with a higher risk of biochemical recurrence, both on univariate and multivariate analysis. However, when the Gleason score was subdivided into 3+4 versus 4+3, the difference in biochemical recurrence of patients with or without a tertiary was not significant. The other, smaller study (214 patients) found that the presence of a tertiary grade 5 was significant on univariate but not multivariate analysis.[26]

A high proportion of prostatic adenocarcinomas are multifocal and there are two methods of grading. One is to look at the totality of the different foci and assign a composite grade by prevalence, and mentioning the tertiary if present. This was the method used in the publications of the largest series investigating the significance of the tertiary grade. [24] The alternative method is to grade the index tumour, which is generally regarded as the tumour of highest stage or, of greatest size if all organ confined. There are insufficient data to clearly identify one method as superior, but the method used should be recorded.

5.2. Staging

Staging using the TNM criteria[1] is mandatory, albeit with some provisos. In particular, as discussed in Section 6 regarding tumour volume measurements, subdividing the category of organ confined tumours (pT2) does not appear to provide useful independent prognostic information.

It should be noted that the pT1 category is limited to biopsies and trans-urethral material, and does not apply to radical prostatectomies, even if unsuspected prostatic carcinoma is identified in cystoprostatectomy specimens for bladder cancer.

The major decision in radical prostatectomy (RP) specimens is to distinguish between tumours limited to the prostate (organ confined, pT2) or involving extraprostatic tissues (pT3). Whilst invasion into seminal vesicles (pT3b) is generally easier to assess, identification of extraprostatic extension (EPE, pT3a), defined as tumour extending beyond the normal confines of the prostate gland,[27] can be problematic.

The prostatic capsule is not a well-defined structure.[28] In the lateral and posterior parts of the gland, it consists of a band of fibromuscular connective tissue that blends imperceptibly with the prostatic stroma. In other areas, such as the apex and the bladder neck, the capsule is not present so that definitions of extra-capsular extension have to be carefully defined. Although there are rare instances of fat within the prostate (usually only one or two adipose cells), involvement of peri-prostatic fat by tumour indicates EPE and thus spread beyond the gland.[29] Tumour involving large nerve bundles in the region of the neurovascular bundles even in the absence of fat involvement is considered EPE. In

addition, tumour that is beyond the normal contour of the prostatic edge involving connective tissue that is typically looser than prostatic stroma is an indicator of EPE.[27] In some instances, bulging tumours are associated with desmoplastic stromal response, and generally this is an indication of EPE. This is particularly important in looking at the anterior region, where the anterior fibromuscular stroma blends into the extraprostatic connective tissue. In this location, tumour that extends beyond the confines of the normal glandular portion of the prostate is considered EPE. The assessment of EPE at the apex is controversial. Because of the common presence of benign glands within skeletal muscle bundles from the urogenital diaphragm, some pathologists contend that EPE cannot be assessed at this site. Others consider the presence of tumour beyond the level of normal prostatic acini or involvement of the inked perpendicular (radial) apical margin if benign glands are not present at that site[30] as indicative of EPE. However, EPE is most commonly seen in peripheral zone tumours posterolaterally; these areas are especially easy to identify if whole mounts are used.

5.2.1. Seminal vesicle involvement

Seminal vesicle involvement (SVI, pT3b) is a poor prognostic factor after radical prostatectomy[31-34] and is commonly associated with EPE. There is much variation in the amount of seminal vesicle type epithelium that is within the prostate gland and invasion of the intraprostatic portion is viewed as ejaculatory duct involvement and not SVI. Carcinoma can invade the extra-prostatic seminal vesicles by spreading along the ejaculatory duct, by direct invasion at the base of the prostate, by extending into peri-seminal vesicle soft tissue and then into the wall of the seminal vesicle or, rarely, via discontinuous metastases.[35] It should be noted that invasion of soft tissues around the seminal vesicles is still classified as EPE (pT3a) unless there is invasion into the stroma of the seminal vesicle.

5.2.2. Bladder neck involvement

Invasion into the bladder neck (identified most readily when there is invasion of detrusor muscle) is classified as pT4 disease in the 2002 TNM system, which would indicate that prognosis is worse than for EPE (pT3a) or seminal vesicle invasion (pT3b).[1] Although one prospective study of 364 patients concluded that bladder neck invasion, controlling for pathological classification, margin status and Gleason score, was an independent predictor of early PSA recurrence,[36] larger, retrospective studies have not confirmed this.[37,38] Outcomes have been reported as better than those of patients with seminal vesicle invasion and similar to those of patients with EPE.[39,40] The International Union against Cancer (UICC) have recently instituted a process of continuous improvement of the TNM system,[41] and the 2002 classification may be modified as a result of these investigations.[1]

5.3. Margin status

Many studies have reported on the prognostic significance of involved margins.[21,42-44] A positive margin is identified when tumour is in contact with an inked surface of the specimen. Because the radical prostatectomy specimen is surrounded by a tiny amount of periprostatic connective tissue, the tumour has to involve the inked surface, and a closely approaching margin should be considered negative.[45]

As detailed in Section 3.2, tumour at an inked margin can be difficult to interpret because of disruption of the specimen either during surgery or subsequent specimen handling. When prostatic cancer at the inked margin is intraprostatic, the designation of stage pT2+ disease is used, indicating that the tumour is essentially organ confined elsewhere, but EPE in the region of the capsular incision cannot be assessed.[44,46] The location of positive margins is required for audit purposes, as a consistent pattern would indicate that changes to surgical technique are required.

There is some indication that the degree of margin positivity is important. Extensive or multifocal positive margins demonstrate a higher risk of relapse than solitary or focal positive margins.[31,33,46]

5.4. Vascular invasion

The presence of vascular invasion has consistently been reported as an independent predictor of biochemical recurrence following radical prostatectomy.[26,47-54]

5.5. Nodal status

Few published data exist on the pathological examination of pelvic lymphadenectomies in patients undergoing radical prostatectomy, but the number of lymph nodes obtained in a lymphadenectomy dissection varies widely. One study reported that a median of 16 nodes (range 5–40) could be detected, and that the rate of cancer detection increased with the number of nodes present, suggesting that a minimum of 13 nodes was required.[55] Such high yields are not the norm in UK practice, but the number present should be recorded. The diameter of the largest metastasis appears to be more predictive of cancer-specific survival than the number of positive nodes alone,[56,57] whereas the presence of extranodal extension was not predictive.[57]

5.6. Summary of core data items

Clinical data:

- type of specimen
- procedure

Macroscopic pathology data:

- specimen weight and measurement in three dimensions
- presence or absence of:
  - fasciae and covering connective tissue
  - incisions into the prostate with locations
  - seminal vesicles and vasa
  - visible tumour and tumour extension beyond the prostate.

Microscopic pathology data:

- Gleason score (by prevalence) and the presence/absence of a tertiary grade (any type)
- TNM stage classification (requires proportion of chips with cancer for TURP specimens)
- margin status and, if positive, their location and extent (radical resections)
- presence or absence of vascular invasion.

If lymphadenectomy performed:

- number of nodes present on each side
- number of positive nodes on each side
- diameter of largest positive node.

6. Non-core data items

6.1. Extent of extra-prostatic extension (pT3a tumours)

The degree of EPE can be subdivided into focal or non-focal.[58] In focal EPE, there are only a few neoplastic glands outside the prostate, whereas more substantial involvement of the periprostatic tissue is seen in non-focal EPE. Not uncommonly, a distinct tongue of tumour extending well into periprostatic connective tissue is seen. However, there is no standardised method of subdividing EPE into focal versus non-focal types, despite the fact that most studies, by their own local methodology, show it to be prognostically significant.[58,59]

6.2. Tumour volume

Recent studies on the significance of tumour volume as an independent, prognostically useful factor are conflicting. Volume correlates with Gleason score, pathologic stage and

margin status. Although the percentage of the RP specimen involved by cancer has been reported to provide predictive information in a multivariate model by some authors,[60,61] this has been disputed by others,[62-64] including a study focussing on Gleason 6 score tumours.[65] Difficulties are compounded by the fact that some centres do not process the entire specimen[66] and, given the multifocal nature of the disease, there are questions about whether all tumours or merely the index tumour should be assessed.[67,68]

The assessment of studies of tumour volume is complicated by the numerous methodologies in use. These include visual extent of tumour,[69] the percentage of carcinoma relative to the overall prostatic volume,[61] more complex grid based estimates[70] and maximum tumour diameter.[71] Because many studies report that tumour volume is not an independent prognostic factor, in line with recent guidelines from other international experts, we suggest that detailed tumour volume measurements in radical prostatectomy specimens is unnecessary.[27,72] However, it is useful to give some indication of tumour extent using visual inspection of the percentage of tissue involved by cancer or other simple methods. If only a small, organ-confined tumour is present, the urologist may advise the patient that he is likely to be cured of his disease. The location of the tumour within the prostate also does not appear to be an independent variable.[30]

6.3. Perineural invasion

Perineural invasion is commonly observed in radical prostatectomy specimens, recorded in 90% of cases when immunocytochemistry is used to increase the detection of nerves.[73] Studies correlating its presence with biochemical recurrence have generally found that it is not independently significant when analysed with other predictive factors such as seminal vesicle or lymphovascular invasion.[73-76] When analysis was restricted to only large diameter nerves (>0.25mm), perineural invasion was independently predictive of worse outcome in a cohort of 640 patients after a median follow-up period of 48 months.[77] A subsequent study that included the diameter and location of the nerves involved did not confirm this, but only 105 patients were included and the median follow-up period was significantly shorter, at 26 months.[73] Further difficulties in interpreting the literature include the retrospective nature of most studies and the absence of information regarding the surgical procedure. For instance, removal of the neurovascular bundle may improve cancer control in patients with perineural invasion, but indications for a nerve-sparing procedure can vary between and within studies.

7. Diagnostic coding

The 6th edition of TNM[1] is recommended for tumour staging (see Appendix A). The main SNOMED codes relating to prostatic disease are summarised in Appendix B.

8. Reporting of biopsy specimens

Cores may be sent to the laboratory as individual specimens or several cores may be placed in one pot. At the very minimum, cores should be separated into right and left sides as the surgical approach may vary depending on side-specific tumour burden.

The majority of biopsies are taken with the 18-gauge biopsy gun under transrectal ultrasound guidance. Handling of prostatic biopsies within the laboratory requires experienced staff and stringent quality control, as the aim is to produce the greatest surface area for examination in order to detect small foci of cancer.[2] Optimising pre-embedding and embedding techniques can reduce the number of levels required and the rate of equivocal diagnoses.[78]

The cores are thinner than biopsies of breast, for instance, and have a tendency to curve and/or fragment. Care must be taken whilst straightening them for processing and embedding. Separation and flattening to subsequently optimise embedding of the cores is

important to identify foci of cancer in individual cores, count the number of positive cores and assess the length of tumour. This can be achieved by using individual cassettes or by sandwiching the cores between two inserts, such as foam pads or nylon meshes,[78] depending on local practice. Cores can be laid out in a specific order to correlate with site of origin. The use of haematoxylin to colour the cores is helpful in identifying them at the embedding stage.

Flat embedding is essential to optimise sectioning and representation of the full length of the core. At least three levels are taken: one from the top half, middle and lower portion of each core. Examining less than three levels may miss significant clinical findings, whether the diagnosis of cancer itself or prognostic features such as grade or perineural invasion.[79] In practice, the greatest problem is cutting too deep into the core for the first level and discarding valuable tissue. Introducing a relatively superficial first section, with three subsequent levels, into the sectioning protocols can circumvent this problem.

Small foci suspicious for carcinoma may only be present at specific levels. Retaining spare sections from each level allows the use of immunocytochemistry to make a definitive diagnosis in difficult cases. This is important to avoid unnecessary re-biopsy; firstly because of the associated morbidity and secondly because subsequent biopsies will not necessarily sample the relevant area in the absence of clear anatomical landmarks on ultrasound. Immunostaining the original H&E section is a possibility, but there are technical difficulties related to sections lifting from non-charged slides.[80]

In addition to the costs of processing and sectioning additional blocks and workload implications, the value of retaining sections for immunocytochemistry makes embedding each core individually impractical in many laboratories. The disadvantages of combining multiple cores in one block are greatly minimised if the techniques described above are employed.

8.1. Quality criteria

The operator performing the biopsies should compare the length of the core with the length of the needle notch to ensure each core is adequate, and repeat the procedure if it is not and the patient can tolerate it.[2] Nevertheless, there are wide, operator-dependent variations in the amount of prostatic tissue sampled even if the same biopsy protocol is employed.[81] In the European Randomised Study of Screening for Prostate Cancer, there was a correlation between the average total amount of prostatic tissue sampled per centre and the cancer detection rate.[81] The length of single cores sampled can vary by more than 3.6-fold, and core length also correlated with the cancer detection rate in this study.[82] Therefore, although there is no minimum set for an adequate biopsy, pathologists should provide some feedback on the amount of prostatic tissue sampled. NHS guidance states that at least 96% of the tissue should consist of prostate[2] and that this should be audited. Reporting the presence of non prostatic tissues (e.g. rectal mucosa) therefore provides valuable feedback and allows the operator to correct his or her technique, improving quality control.

8.2. Gleason grading

The International Society of Urological Pathologists (ISUP)[22] proposed a modification to the method of reporting the sum score on biopsy material if a tertiary pattern was present. The evidence provided for making the change appeared to be scant and prompted a systematic evidence review,[24] which showed that the available data, derived from radical prostatectomy specimens, the presence of a tertiary grade, whether higher or lower, is associated with a higher risk of biochemical recurrence. However, the review revealed differences in the interpretation of the original Gleason scoring system, which has distorted the available literature.

The original publications describing the Gleason system emphasised the recording of the predominant (by area) and lesser (by area) grade.[83-86] The only variation occurred when

there was a large difference between different biopsies from a given patient. Then, it was stated that the composite grade was adjusted to indicate the extremes, suggesting that the lowest and highest grades were selected. It was only two decades later, in a textbook chapter,[87] that Gleason described the algorithms that were used to reduce the very few tumours with three or more grades to two grades. In radical prostatectomies and transurethral resections, the highest and lowest grades were recorded if they each represented over 5% of the tumour, regardless of the extent of the middle grade. However, in biopsies, he stated that the two highest grades were recorded to avoid sampling error. These details were not given in the original papers and it would seem that, since then, there have been variable interpretations of the method used to take a tertiary grade into account. The 5% rule appears to have been either applied to all specimen types, or not applied at all. Although it was quite clear from the Gleason papers that all different grades (up to two), regardless of extent, should be included in the score, some pathologists have doubled the primary score and ignored the secondary if less than 5% of the total. These pathologists would therefore report a case as Gleason 3+3 with a tertiary grade 4, if grade 4 represented less than 5% of the total tumour present, whereas other pathologists, applying the original Gleason rules, would report this as Gleason 3+4. This variation in practice makes the literature on the significance of a tertiary grade difficult to interpret, particularly when cases originally reported by a multiplicity of pathologists have been retrieved from files.[23,88]

In keeping with Gleason's original papers and recent available evidence,[89] the presence of a secondary grade 4 or 5, even if the primary grade 3 is very extensive, should always be reported as such, and not as a tertiary grade. This is in line with the ISUP recommendations,[22] and will probably result in a reduction of the frequency of tertiary grade reports in many laboratories. The controversy remains for cases where the primary grade is either 4 or 5, and the secondary grade is 3. ISUP recommends reporting the secondary grade if carcinoma is extensive but ignoring if only a small amount of cancer is present. This is very difficult to apply in practice, particularly since the required amounts of cancer have not been defined. Given the absence of evidence, it seems more sensible to apply the same rule for both situations, bearing in mind that it is established that a primary grade of 4 or 5 is associated with poorer prognosis in any case.[90]

In terms of incorporating the tertiary grade in the sum score if it is higher than the primary or secondary grade defined by area, only one paper, published since the systematic review, has provided evidence for biopsy material.[91] The biopsies of 2379 men were reviewed by an experienced genitourinary pathologist and the results correlated with biochemical recurrence following radical prostatectomy or radiotherapy. There were no cases of Gleason score 6 or less with a tertiary pattern 4 or 5 and only 36 cases (1.5%) of Gleason score 7 with tertiary grade 5. The estimated risk of biochemical recurrence for these 36 patients was similar to that of patients with Gleason 8–10 and higher than the estimated risk for Gleason 7 without tertiary 5. Therefore the inclusion of the higher grade would appear to be valid, but there are some important caveats.

Firstly, a tertiary Gleason grade 5 is rare in experienced hands. In the papers specifically looking for grade 5 in radical prostatectomy specimens with Gleason 7, the frequency was 13[25] and 17%.[26] In the only biopsy paper,[91] it was even lower, at 1.5%. Clearly EQA schemes cannot address prevalence, but data from the NHS Prostate Pathology EQA scheme shows that a tertiary grade is identified more often by general pathologists than by the specialist group. Secondly, published reports on inter-observer variability indicates that agreement is worst for the presence or type of tertiary grade, compared with primary or secondary, failing to reach even moderate agreement for expert uropathologists. To avoid overdiagnosis of a tertiary grade 5 and the consequent overestimation of risk, it is essential that pathologists are aware of the relative infrequency of a tertiary grade 5 in biopsy material, and the inherent diagnostic difficulties. Otherwise, overestimation of the score would have serious repercussions on patient management.

ISUP recommends assigning a Gleason score to every 'specimen' but recognises the difficulties particularly if multiple biopsies are submitted in a single cassette and have fragmented. However, it also gives the option of creating a 'global' or composite Gleason score for the case. It defers to the clinician whether the global Gleason score or the 'highest' Gleason score should be used. Discordance between composite and highest Gleason scores are relatively infrequent, and usually occur because one core contains only high grade Gleason (eg 4+4) whereas all the other cores contain a lower grade (eg 3+4). Unfortunately, at present, there is insufficient data to suggest the optimal method for predicting the 'actual' Gleason score of the tumour. We therefore recommend that as a minimum, a composite score ought to be given in the final conclusion. Noting any variations in Gleason score in individual cores is helpful to establish the final score, and locally clinicians may wish to use the more specific information for treatment planning (for instance non nerve sparing RP on the side of the highest score).

8.3. Tumour extent

Estimates of tumour extent are used in a number of predictive tools for outcomes (stage or recurrence) in prostate cancer.[92]

The number of positive cores appears to improve prediction of biochemical recurrence, whereas the percentage of cores is a better predictor of pathological stage.[93] There are also data to suggest that the percentage of positive cores on the dominant side has stronger independent predictive value than the total percentage.[94]

In terms of the significance of linear extent of cancer, two systematic reviews were conducted in preparation of this dataset. The first addressed the issue of 'microfocal' carcinoma.[95] The definition of small volume carcinoma varied widely, but even using the most stringent (only a few malignant glands in one core) or common (less than 3 mm of cancer in a single core, no Gleason grade 4 or 5), there was a significant risk of progressive disease even after radical surgery or radiotherapy.

The second addressed the prognostic value of linear measurements of tumour extent in general.[96] The amount of carcinoma as a percentage of overall prostatic tissue was established as an independent predictor of cancer-specific survival[97] in untreated or conservatively treated men, indicating that linear tumour measures are potential prognostic factors and not just predictive of response to one form of therapy. The weight of current evidence suggests that the percentage of cancer on biopsy may be more valuable in predicting PSA recurrence compared to the number of positive cores alone. The review found consistent data to support the use of either the total percentage of cancer (TPC) or the greatest percentage of cancer in any one core (GPC), both methods providing similar hazard ratios. Hazard ratios appeared to become more significant if intervening benign tissue was excluded for the GPC estimation. Results for absolute measurements (length in mm) were inconclusive.

The TPC is the ratio between the total amount of cancer and the total amount tissue sampled, so will therefore be strongly influenced by the latter. This may underestimate large tumours if they are unilateral or if additional centrally rather than peripherally directed biopsies are taken, as these do not generally increase cancer yield.[98] To estimate the GPC, first the core with the greatest amount of cancer is selected and the total length of cancer (excluding intervening benign tissue) relative to the total length of the core is assessed. This may underestimate tumour burden if multiple cores are involved.

The recent NICE guidance[4] included pathological criteria for the selection of patients for active surveillance. In addition to clinical stage T1c and a PSA density of less than 0.15ng/ml/ml, these were:

- Gleason score 3+3=6
- cancer in less than 50% of the total number of biopsy cores

- less than 10 mm of any core involved.

Systematic review has failed to reveal any evidence that this combination of criteria has been tested. The two validated predictive models use TPC[99] or GPC[100] and serum PSA not PSA density. As neither model appears to be superior, the most reproducible and least time-consuming method would be best applied in clinical practice. This is currently being evaluated in the NHS Prostatic Pathology EQA Scheme.

In the meantime, pathologists are encouraged to use one or other method, if not both, and to gather data prospectively and audit outcomes.

8.4. Perineural invasion

A systematic review was undertaken to clarify the significance of perineural invasion in prostatic biopsies.[101] Perineural invasion is common in advanced disease and is not of prognostic significance. However, in clinically localised disease, the balance of evidence indicates that perineural invasion is independently significant, particularly if large or multiple nerves are involved. Active surveillance may be a less attractive option for these patients.[101] Nerves are not necessarily present in biopsy material, and it is therefore not always possible to assess the possibility of perineural invasion.

8.5. Vascular invasion

This is not commonly seen in localised disease. Given that the presence of vascular invasion in radical prostatectomy specimens is reported as an independent predictor of biochemical recurrence,[26,47-54] it is likely to be of significance in biopsies, although specific data are scant.

8.6. Invasion into periprostatic tissues

Small groups of adipose cells are very rarely seen within the prostate, therefore the presence of tumour in fat is generally indicative of EPE.

8.7. Summary of biopsy data items

Clinical data:

- number and site of prostatic biopsies
- history of previous treatment
- history of previous biopsies.

Macroscopic pathology data:

- number of cores or fragments
- length of cores.

Microscopic pathology data:

- Gleason sum score:
    - If only one grade is present, it is doubled (e.g. 3+3);
    - If two grades are present, both are included by order of prevalence;
    - If more than two grades are present, the third is included in the sum score if it is of higher grade.
- the presence of a tertiary grade
- the number and percentage of cores positive per side
- the total percentage or the greatest percentage of cancer (or both)
- perineural invasion, if present
- vascular invasion, if present
- involvement of adipose tissue if present

- if no carcinoma is present, any features that should lead to consideration of re-biopsy, including:
  - high grade prostatic intraepithelial neoplasia
  - foci suspicious for but not diagnostic of carcinoma
- For quality assurance of biopsy technique: presence of non-prostatic tissues (e.g. rectal mucosa).

9. Reporting of frozen sections

Frozen sections were regularly performed to assess nodal status during radical prostatectomy in the 1990s, until it became clear that the false negative rate could be as high as 33%.[102] In parallel, the refinement of predictive tables for the risk of lymph node metastasis relative to biopsy Gleason score and presenting PSA reduced the necessity for pre- or peri-operative nodal examination.[90] As a result, frozen sections are rarely performed in routine practice.

Frozen sections can occasionally be requested to assess margin status at the bladder neck or the neurovascular bundles. The finding of carcinoma will then prompt a further excision at the bladder neck or complete excision of the affected neurovascular bundle. However, the yield of positive results is too low to justify frozen sections in routine practice,[103] although it can be helpful in high-risk cases.[104]

10. Adjuncts to diagnosis: immunocytochemistry

Immunochemistry is an important adjunct to accurate prostatic cancer diagnosis in the differentiation of prostate cancer from another tumour, the investigation of differentiation patterns within a prostatic cancer and the examination of suspicious acini.

10.1. Differentiation of prostate cancer from another tumour type

Identification of the prostatic origin of a poorly differentiated primary or metastatic carcinoma is important because prostate cancer, even in advanced stages, may respond to hormonal manipulation. Serum prostate specific antigen (PSA) may help to establish the prostatic origin of poorly differentiated carcinomas. However, some tumours, although expressing PSA immunohistochemically, may secrete only small amounts into the blood. Also, because PSA production and mitotic activity are mutually exclusive, high-grade tumours may not be associated with high serum PSA levels. Finally, urothelial carcinomas extending into the prostate gland are often associated with raised serum PSA.

Immunohistochemistry for PSA and prostate specific acid phosphatase (PSAP) remains the definitive method for establishing the diagnosis in morphologically difficult cases. Several studies report the specific nature of both PSA and PSAP.[105,106] Both polyclonal and monoclonal anti-PSA antibodies are in use in the UK.[107] The monoclonal anti-PSA antibody is less sensitive in the identification of poorly differentiated prostate cancer.[108] No comparison of the sensitivity of monoclonal and polyclonal anti-PSAP antibodies in high-grade prostate cancer has been reported. However, two studies found PSAP to be more sensitive (though slightly less specific) than PSA in high-grade prostate cancer.[109,110] Because the distinction of prostate cancer from other tumours, such as urothelial carcinoma, has important therapeutic implications, an immunohistochemical panel including both markers is generally recommended. The selection of tissue for use as a positive control is also important because the use of too strongly positive tissue could mean that the lack of staining sensitivity is overlooked. It is known that PSA and PSAP expression is much higher in benign prostate glands and low-grade prostate cancer than in high-grade prostate cancer. In view of this variability, multiblocks containing benign prostate, well/moderately differentiated prostate cancer and poorly differentiated prostate cancer may provide the

ideal positive control for prostate-specific antigen and prostate-specific acid phosphatase immunohistochemistry.[107]

10.2. Differentiation patterns within prostatic cancer

The vast majority of prostatic malignancies are adenocarcinomas. Rarely sarcomas may arise requiring immunochemistry. The identification of neuroendocrine changes, especially if of oat cell type, is important as these may be treated in a different manner.[111] Morphology may be backed up with CD56, chromogranin, synaptophysin or other neuroendocrine markers, though PSA and PSAP may be negative.[112] Occasionally tumours will secrete endocrine factors such as adrenocorticotropic hormone (ACTH) and wider panels may be useful.[113]

10.3. The examination of suspicious acini

It is well established that prostatic cancers lack basal cells, but so do a small proportion of benign glands. Therefore the absence of demonstrable basal cells is an additional, rather than absolute, factor supportive of malignancy, and must be interpreted together with the morphological appearances.

Distinction of basal cells may be difficult using routine stains. A number of prostatic basal cell markers are currently available. In the UK, the most widely used basal cell marker is the high-molecular weight cytokeratin antibody clone 34bE12. Cytokeratin 5/6 and LP34 are also used, while p63 is used less often but probably is increasing in use.[114] 34bE12 has been extensively studied and validated in the literature.[115,116] In contrast, the infrequently used p63 has only relatively recently been established as a basal cell marker.[117,118] There is a wide variation in the use of basal cell markers, which reflects the paucity of studies comparing them and providing guidance regarding their relative usefulness and efficacy.

One study has reported cytokeratin 5/6 to be marginally more sensitive than 34bE12.[119] Another study found LP34 to be slightly more sensitive than cytokeratin 5/6, but the panel of markers studied did not include 34bE12.[120] Also, unlike other basal cell markers, LP34 may react with the secretory cells of the prostate gland, making interpretation difficult. The advantages of p63 has been advocated by others.[121,122] However, it is generally recognised that none of the basal cell markers are absolutely sensitive, as a small proportion of benign glands are negative with each of these markers. Using a combination of basal cell markers has been shown to increase the sensitivity of immunostaining,[123] although the ideal combination is uncertain. P63, a homologue of p53, displays nuclear immunoreactivity. Therefore, using one of the high-molecular weight cytokeratins antibodies with p63 may be advantageous.

A major disadvantage of the basal cell markers is that it relies on a negative result to support the diagnosis of cancer. On the other hand, alpha methylacyl coenzyme A racemase (AMACR) was detected through a cDNA subtraction analysis showing that it was overexpressed in a high proportion of prostate cancers relative to benign tissue,[124,125] although it was also over-expressed in 25% of normal tissues.[125] AMACR is involved in peroxisomal beta-oxidation of branched-chain fatty acids, and the granular luminal cytoplasmic positivity is distinctive. Recent studies have confirmed that AMACR is neither as sensitive nor specific as the initial studies indicated.[126-128] Reported wide variations in specificity in the literature may be due to differing methods of antigen retrieval or whether polyclonal or monoclonal primary antibodies are used.[129] The use of AMACR in routine practice is still open to question, although some use it in cocktails with basal cell markers.[130] In the context of small foci suspicious of malignancy, together with appropriate H&E morphology and basal cell markers, demonstration of AMACR expression may help confirm a diagnosis of cancer. However, prostatic intraepithelial neoplasia (PIN) also expresses AMACR, with high levels more closely associated with invasive carcinoma.[131] Following treatment, AMACR may be negative in hormone controlled prostate cancer but is positive in hormone escaped metastatic prostate cancer.[132] It remains positive after radiation.[133]

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12. Acknowledgments

The authors are grateful to Bernadette Coles and Malcolm Mason for their contribution to the evidence reviews prepared for this dataset. We thank Cancer Research Wales for funding some salaried work and library facilities. The support of the Prostate Cancer Risk Management Group in general, and Julietta Patnick and Richard Winder in particular, have been invaluable. We also thank Cancer Research UK for supporting P Harnden.

The authors gratefully acknowledge the contribution of Dr Brian Naylor, Consultant Pathologist (retired), Airedale General Hospital, Keighley, in preparing this dataset.

Appendix A TNM pathological staging (6th edition, UICC[1])

The major change in the 6th edition[1] affects the assessment of nodes and applies to all cancer sites. A tumour nodule in the connective tissue of the lymph drainage area is classified as a regional lymph node metastasis if the nodule has the form and smooth contour of a lymph node, even in the absence of histologically proven residual lymph node tissue.

pT – Primary tumour

pTx Primary tumour cannot be assessed

pT0 No evidence of primary tumour

pT1 Clinically inapparent tumour not palpable or visible by imaging
- pT1a Tumour incidental histological finding in 5% or less of tissue resected
- pT1b Tumour incidental histological finding in more than 5% of tissue resected
- pT1c Tumour identified by needle biopsy (e.g. because of elevated PSA)

pT2 Tumour confined within prostate[1]
- pT2a Tumour involves one half of one lobe or less
- pT2b Tumour involves more than half of one lobe, but not both lobes
- pT2c Tumour involves both lobes

pT3 Tumour extends through the prostate capsule[2]
- pT3a Extracapsular extension (unilateral or bilateral)
- pT3b Tumour invades seminal vesicle(s)

pT4 Tumour is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, or pelvic wall.

Notes

1. Tumour found in one or both lobes by needle biopsy, but not palpable or visible by imaging, is classified as T1c.
2. Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as T3, but as T2.

pN – Regional lymph nodes

pNx Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 Regional lymph node metastasis

pM – Distant metastasis

pMX Distant metastasis cannot be assessed

pM0 No distant metastasis

pM1 Distant metastasis
- pM1a Non-regional lymph node(s)
- pM1b Bone(s)
- pM1c Other site(s)

Stage grouping

Stage I	T1a	N0	M0	G1
Stage II	T1a	N0	M0	G2, 3–4
	T1b,c	N0	M0	Any G
	T1, T2	N0	M0	Any G
Stage III	T3	N0	M0	Any G
Stage IV	T4	N0	M0	Any G
	Any T	N1	M0	Any G
	Any T	Any N	M1	Any G

Appendix B SNOMED ‘T’ and ‘M’ codes

SNOMED ‘T’ codes

Right-sided biopsies	T77220
Left sided biopsies	T 77230
Radical prostatectomy	T77100
Lymph nodes	T08000

SNOMED ‘M’ codes

No evidence of malignancy	M09450
High-grade prostatic intraepithelial neoplasia	M81402
Suspicious for malignancy	M69760
Adenocarcinoma	M81403
Metastatic adenocarcinoma	M81406

Appendix C Reporting proforma for transurethral resections of prostate

Surname		Forenames		Date of birth				
Hospital		Hospital no		NHS no				
Date received		Date reported		Report no				
Pathologist		Surgeon		**Review**	**Yes**	□	**No**	□

Nature of specimen(s) and core macroscopic items

TURP	□	Weight: g	Proportion sampled:
Enucleation	□	Weight: g	Dimensions x x mm

Core microscopic items

Tumour type	Microacinar	□	Other (please specify)	
Percentage of tumour if clinically unsuspected tumour			(number positive/total x100)	
Gleason score	Primary grade		Secondary grade	
	Tertiary grade		No tertiary grade	□
Vascular invasion	Absent	□	Present	□

pT category (TNM 2002)	pT1a	□	Incidental carcinoma in 5% or less of tissue resected
	pT1b	□	Incidental carcinoma over 5% of tissue resected

SNOMED codes	
T	M
T	M

Signature of pathologist…… Date……..

Appendix D Reporting proforma for radical prostatectomies

Surname		Forenames		Date of birth					
Hospital		Hospital no		NHS no					
Date received		Date reported		Report no					
Pathologist		Surgeon		**Review**	**Yes**	□	**No**	□	

Nature of specimen(s) and core macroscopic items

Prostate	Weight: g			Dimensions: mm apex-base, mm antero-posterior, lateral								
	Fasciae/connective tissue			Present □		Absent □		Comments:				
	Surgical incisions			Present □		Absent □		Location(s) if present:				
Seminal vesicles	Right	N/A	□	Present	□	Dimensions	x	x	mm, vas	mm		
	Left	N/A	□	Present	□	Dimensions	x	x	mm, vas	mm		
Lymph nodes	Right	N/A	□	Present	□	Dimensions	x	x	mm			
	Left	N/A	□	Present	□	Dimensions	x	x	mm			

Core microscopic items

Tumour type	Microacinar	□	Other (specify)			No tumour □	
Gleason score (prevalence)	Primary grade		Secondary grade				
	Tertiary grade		No tertiary grade	□			
Organ confined	Yes	□	No	□			
Beyond the outline of the prostate	Yes	□	No	□			
Into seminal vesicle(s).	Yes	□	No	□			
Into bladder neck	Yes	□	No	□			
Fixed or into adjacent organs or pelvic wall.	Yes	□	No	□	Specify:		
Margin status	Negative	□	Positive	□	Location(s) Intraprostatic Yes □ No □ Apex □ Base □ Circumferential □		
Vascular invasion	Absent	□	Present	□			

Nodal status	No nodes present	□			
	Node negative	□	Number	Right side	Left side
	Node positive	□	Number (positive nodes/total)	Right side /	Left side /
				Maximum dimension mm	Maximum dimension mm

pTNM stage 2002			**SNOMED codes**	
pT	pN	pM	T	M
□ pT2 (organ confined) □ pT3a (EPE) □ pT3b (SV positive) □ pT4 (other organs involved)	□ pNx □ pN0 □ pN1		T	M

Signature of pathologist…… Date……..

Appendix E Reporting proforma for prostatic biopsies

Surname		Forenames		Date of birth					
Hospital		Hospital no		NHS no					
Date received		Date reported		Report no					
Pathologist		Surgeon		**Review**	**Yes**	□	**No**	□	

Nature of specimen(s) and core macroscopic items

Right side (specific locations below if applicable)	Number	Length	Left side (specific locations below if applicable)	Number	Length

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Core microscopic items

Tumour type	Microacinar	□	Other (please specify)						
Gleason score	Primary grade		Secondary grade						
	Tertiary grade		No tertiary grade	□					
Number of cores positive/total	Right side	/	Left side	/					
Other estimates of tumour extent	Greatest percentage of cancer (single most involved core) % Side: Right □ Left □ Both □		Total percentage of cancer (sum cancer lengths/sum core lengthsx100) % Right % Left %						
Perineural invasion	N/A	□	Invasion	□	Right	□	Left	□	
Invasion into adipose tissue	N/A	□	Invasion	□	Right	□	Left	□	
Vascular invasion	N/A	□	Present	□					
Non prostatic tissues	N/A	□	Present	□	Type:				

SNOMED codes	
T	M
T	M

Signature of pathologist…… Date……..