Published in final edited form as:

Virchows Arch. 2010 November ; 457(5): . doi:10.1007/s00428-010-0971-z.

Measurements of cancer extent in a conservatively treated prostate cancer biopsy cohort

Ramzi Rajab,

Centre for Molecular Oncology and Imaging, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Gabrielle Fisher,

Cancer Research UK Department of Epidemiology, Mathematics and Statistics, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK

Michael W. Kattan,

Department of Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, OH, USA

Christopher S. Foster,

Department of Cellular Pathology and Molecular Genetics, Liverpool University Hospital, Liverpool, UK

Tim Oliver,

Centre for Molecular Oncology and Imaging, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Henrik Møller,

King's College London, Thames Cancer Registry, London, UK

Victor Reuter,

Departments of Pathology and Urology, Memorial Sloan Kettering Cancer Centre, New York, USA

Peter Scardino,

Departments of Pathology and Urology, Memorial Sloan Kettering Cancer Centre, New York, USA

Jack Cuzick, and

Cancer Research UK Department of Epidemiology, Mathematics and Statistics, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK

Daniel M. Berney on behalf of the Transatlantic Prostate Group

Centre for Molecular Oncology and Imaging, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK

Centre for Molecular Oncology and Imaging St. Bartholomew's Medical School, Queen Mary, University of London, Charterhouse Square, London EC1M 6BQ, UK

Daniel M. Berney: D.Berney@bartsandthelondon.nhs.uk

Abstract

© Springer-Verlag 2010

Correspondence to: Daniel M. Berney, D.Berney@bartsandthelondon.nhs.uk.

Conflict of interest statement We declare that we have no conflict of interest.

The optimal method for measuring cancer extent in prostate biopsy specimens is unknown. Seven hundred forty-four patients diagnosed between 1990 and 1996 with prostate cancer and managed conservatively were identified. The clinical end point was death from prostate cancer. The extent of cancer was measured in terms of number of cancer cores (NCC), percentage of cores with cancer (PCC), total length of cancer (LCC) and percentage length of cancer in the cores (PLC). These were correlated with prostate cancer mortality, in univariate and multivariate analysis including Gleason score and prostate-specific antigen (PSA). All extent of cancer variables were significant predictors of prostate cancer death on univariate analysis: NCC, hazard ratio (HR)=1.15, 95% confidence interval (CI)=1.04–1.28, $P=0.011$; PPC, HR=1.01, 95% CI=1.01–1.02, $P<0.0001$; LCC, HR=1.02, 95% CI=1.01–1.03, $P=0.002$; PLC, HR=1.01, 95% CI=1.01–1.02, $P=0.0001$. In multivariate analysis including Gleason score and baseline PSA, PCC and PLC were both independently significant $P=0.004$ and $P=0.012$, respectively, and added further information to that provided by PSA and Gleason score, whereas NCC and LCC were no longer significant ($P=0.5$ and $P=0.3$ respectively). In a final model, including both extent of cancer variables, PCC was the stronger, adding more value than PLC (χ^2 (1df)=7.8, $P=0.005$, χ^2 (1df)=0.5, $P=0.48$ respectively). Measurements of disease burden in needle biopsy specimens are significant predictors of prostate-cancer-related death. The percentage of positive cores appeared the strongest predictor and was stronger than percentage length of cancer in the cores.

Keywords

Prostate biopsy; Prostate cancer; Biopsy; prognostic factors; Tumour extent

Introduction

The advent of prostate-specific antigen (PSA) screening has resulted in an increase in the detection of early stage tumours [1–3]. However, the benefits of radical therapy in patients with low- or intermediate-risk disease are not clear cut, and many of these patients may benefit from a more conservative approach [4]. Nomograms based on preclinical parameters have been devised to guide clinical management [5–8], but these do not routinely include measures of cancer extent.

Pathological data from biopsy specimens other than Gleason score have increasingly been used to improve the predictive accuracy of outcome models that guide clinical management, by identifying factors associated with an increased risk of disease progression in terms of PSA failure and metastatic disease post-radical prostatectomy [6, 9–14].

A cohort study by the Transatlantic Prostate Group developed a model using Gleason score and PSA to stratify patients with localised prostate cancer managed conservatively into three groups with 10-year cancer-specific mortalities of <10%, 10–30% and >30% [6]. After Gleason score and PSA, the extent of cancer in the biopsy specimen showed a strong association with prostate-cancer-related deaths on univariate and multivariate analysis. However, there are different methods of measuring cancer extent in prostate needle core biopsies. In this study, we determine which pathological assessment of the “extent of cancer” in diagnostic prostate biopsies best predicts long-term survival.

Methods

Study population, follow-up and end points

The protocol for patient selection and data collection methodology has been detailed in a previous report by the Transatlantic Prostate Group [6] and is summarised below. Patients diagnosed with biopsy-proven, localised prostate cancer between 1990 and 1996 were

identified by participating UK cancer registries. Exclusion criteria included age >76 years, no baseline PSA, invasive carcinoma within 5 years prior to diagnosis, hormone treatment prior to biopsy and a follow-up period of less than 6 months. Patients were also excluded if they underwent radical prostatectomy or radiotherapy within 6 months of diagnosis or had evidence of metastasis, a baseline PSA >100 ng/ml or died within 6 months of diagnosis.

The clinical end point was defined as death from prostate cancer. Survival outcomes were ascertained from medical records and cancer registry data. Last follow-up was via the cancer registries, and the last review took place in December 2006.

Pathological assessment of biopsy specimens

Diagnostic needle core biopsy specimens were reviewed by an expert panel of urological pathologists to confirm the diagnosis and Gleason grading. Extent of cancer in biopsy specimens was determined by multiple methods (Table 1): data available included total number of cores (TNC) and number of cores with cancer (NCC) as well as the total length of all cores (TLC) and length of cancer in cores (LCC). Apart from the NCC and LCC, these data allowed calculation of the percentage of cancer-positive cores ($PCC = NCC/TNC$) and secondly the percentage length of cancer (PLC) in the cores ($PLC = LCC/TLC$). Measurements of cancer length and core lengths were all made by an expert uropathologist (DB) with microscope-mounted Vernier's scales and rulers, respectively. Measurements of linear cancer length within individual cores did not include intervening non-tumour tissue. Gleason grading conformed to modern ISUP criteria [15].

Statistics

The primary end point for this study was death from prostate cancer. Univariate and multivariate analyses were performed by proportional hazard models. All *P* values were two-sided and 95% confidence intervals were based on normal distribution.

Results

Patient selection identified a cohort of 2,333 eligible men. Centrally reviewed, Gleason grading results were available for 1,656 (71%) cases, 474 cases were excluded on histological grounds (missing histology 284, incorrect pathological specimen 43, histologically negative 135, no tissue left in the block 6 and six cases were histologically ungradable for Gleason score) and for 203 cases the histology specimen was not requested for review. Cases diagnosed from prostate chips were not included in this study, and analysis was confined to the 744 cases diagnosed on the basis of needle core biopsies. The mean age at diagnosis was 69.2 years (range 44–76 years). Median follow-up was 106 months (range 6–197 months).

The total number of cores per patient ranged from one to nine, and the proportion positive is shown (Fig. 1). In univariate analysis, NCC was a significant predictor of prostate cancer death (hazard ratio (HR)=1.15, 95% confidence interval (CI)=1.04–1.28, χ^2 (1df)=6.4, *P*=0.011) but was less informative than the PCC (HR=1.01, 95% CI=1.01–1.02, χ^2 (1df)=27.1, *P*<0.0001). The KM survivor curve for PPC analysed in three groups (<50%, 50 to <100% or 100%) is shown in Fig. 2a.

In multivariate analysis, in the standard model including Gleason score (5, 6, 7, 8, 9 or 10) and PSA (ng/ml) (0–4, >4–10, >10–25, >25–50, >50–100), PCC was significant independently of Gleason score and PSA and provided additional prognostic value ($\Delta\chi^2$ (1df)=8.1, *P*=0.04). In contrast, NCC provided almost no additional prognostic value ($\Delta\chi^2$ (1df)=0.45, *P*=0.5), Table 2.

The extent of cancer measured as the absolute (LCC) and percentage length of cancer in the needle cores (PLC) was recorded for 737 cases. In univariate analysis, PLC was a significant predictor of prostate cancer death, when assessed as a continuous variable (HR=1.01, 95% CI=1.01–1.02 χ^2 (1df)=21.26, $P=0.0001$) or as a grouped variable. The most informative grouping was based on quintiles (χ^2 (1df)=27, $P<0.0001$) (Fig. 2b), but this was only slightly more informative than a simpler variable based on two groups ($\leq 30\%$, $>30\%$) (HR=2.21, 95% CI=1.6–3.1, χ^2 (1df)=25, $P<0.0001$) (Fig. 2c). Although LCC was also a significant predictor of prostate cancer death, it was less informative (HR=1.02, 95% CI=1.01–1.03, χ^2 (1df)=9.8, $P=0.002$).

In multivariate analysis, PLC was significant independently of Gleason score and PSA and provided some additional prognostic value to the standard model. The added value of the PLC variable based on two groups ($\leq 30\%$, $>30\%$) was very similar to that based on quintiles ($\Delta\chi^2$ (1df), 5.6, $P=0.018$, and $\Delta\chi^2$ (1df), 6.3, $P=0.012$ respectively), but LCC provided almost no additional prognostic value ($\Delta\chi^2$ (1df), 0.96, $P=0.33$) (Table 2).

An analysis of the 723 cases with both extent of cancer variables (PCC and PLC) available allowed a direct comparison of their predictive power. The predictive power of the variable PCC ($<50\%$, 50% to $<100\%$ or 100%) was greater than that of PLC measured either as a two- or five-group variable ($\Delta\chi^2$ (1df)=7.8, $P=0.005$, $\Delta\chi^2$ (1df)=4.5, $P=0.03$, $\Delta\chi^2$ (1df), 4.2, $P=0.04$), respectively (Table 2).

Detailed multivariate analysis for the final model including PCC, Gleason score (<7 , $=7$, >7) and baseline PSA (ng/ml) (0–4, >4 –10, >10 –25, >25 –50, >50 –100) is shown in Table 3.

Discussion

The present dilemma arising out of the advent of PSA screening is how best to manage the increasing proportion of patients with intermediate- and low-risk prostate cancer, as defined by standard models using age, PSA and Gleason score. This is recognition that many of these patients have indolent disease in whom the benefits of radical prostatectomy do not outweigh the surgical morbidity. The parameters that define these two groups are becoming more stringent as clinicians adopt more conservative management protocols [16, 17]. However, even with standard models of prognostication, there is heterogeneity within the low–intermediate-risk (Gleason 6 and 7 and low PSA) patient groups and a recognition that a proportion of patients will develop progressive disease in whom radical treatment is then warranted [18].

This has driven the exploration of pathological factors in preoperative specimens to predict poor outcome. In the absence of validated molecular markers of prognostic value, which are practical in large screening populations, many studies have focused on measurements of disease burden in needle core biopsies.

The number of positive cores in sextant biopsies have been shown to correlate with tumour stage [19–22] and surgical margin status in radical prostatectomy specimens [23, 24] and the presence pelvic lymph node metastasis [25]. Similarly, the percentage of positive cores has been shown to be predictive of stage [26], extra-capsular extension [27, 28], distant metastasis, biochemical progression and death following radical prostatectomy [29].

In addition, the percentage cancer involvement of biopsies is predictive of capsular perforation and seminal vesicle involvement [30]. The total length of cancer has also been shown to correlate with stage, positive surgical margins and biochemical recurrence following radical prostatectomy, respectively [24]. Brimo et al. showed that the greatest

percentage of cancer, the total percentage of cancer and the greatest millimetric length of cancer in the needle cores were closely associated with clinical stage [31].

A systematic review by Harnden et al. determined the significance of measurements of disease burden in biopsy specimens for predicting risk of progression after radical prostatectomy [32]. The authors were unable to make firm conclusions on absolute measurements made of tumour burden. Tumour burden represented as a percentage was found to be more consistent, and most studies they reviewed showed that the percentage of cancer involvement was an independent predictor of PSA recurrence following radical prostatectomy.

In the current study, the percentage of positive cores (FC) was strongly predictive of prostate cancer death over the long follow-up period (median follow-up 117 months) despite the heterogeneity of the study population with regard to standard prognostic indicators (age, PSA and Gleason score at presentation) and treatment-related factors (initial hormone treatment). These findings are consistent with previous studies in which the percentage of positive cores was predictive of stage, surgical margin status [33] and biochemical recurrence [10, 34–37].

The utility of the percentage of positive cores is dependant on the number of cores taken to sample disease extent, which acts as a corrective factor for the size of the gland. Thus, the accuracy of this measure increases with the number of cores taken. In this sense, the measure is likely to overestimate disease extent when the core number is low.

Conversely, when the core number is high (approaching 21 biopsies) and the fraction of positive cores is low, the measurement will more accurately predict low disease burden which is especially important during selection of patients for active surveillance programmes [38]. As only 10% of the cohort was composed of sextant biopsies, there were too few cases to analyse adequately. There was no heterogeneity within this subset of cases. It is hoped that a more contemporary cohort conforming more to modern practice will be published in the future.

Similar principles apply with measurements of the total fractional length of cancer in biopsy specimens. In this study, the power of the total fractional length of cancer in needle biopsies was almost uninformative. This may be explained by the measurement underestimating the size of large tumours when the biopsy number is low and thus may not reflect its true clinical usefulness in predicting prognosis. In fact, several studies have shown that the total percentage length of cancer was predictive of pathological stage and PSA recurrence post-radical prostatectomy [11, 24, 39]. However, other studies also failed to demonstrate a correlation between the percentage of prostate cancer in the biopsy and clinical stage or biochemical recurrence following radical prostatectomy [40, 41].

Limiting factors in this study include its retrospective nature, low biopsy numbers compared to contemporary series and the heterogeneity of the study population when analysing the significance of disease burden in the biopsies. However, despite the aforementioned confounding factors, no contemporary series, let alone one with in which patients are managed by watchful waiting, has enough follow-up to make long-term measurements of this nature. Furthermore, direct comparisons of predicted PSA failure after radical prostatectomy and prostate-cancer-related death in patients managed by watchful waiting or active surveillance need to be made with caution, as PSA failure does not necessarily imply clinical progression without correction for PSA doubling time [42–44].

Conclusions

This study is unique in correlating measurements of disease burden in diagnostic specimens with long-term survival in patients managed by watchful waiting. The percentage of positive cores was strongly predictive of prostate-cancer-related death on multivariate analysis and added additional information to models utilising PSA and Gleason score to refine management decision in patients with low-risk disease who would qualify for conservative management.

Acknowledgments

This study was supported by Cancer Research UK, a Specialised Programme of Research Excellence (SPORE) grant from the US National Cancer Institute (USA), Orchid and The David Koch Foundation. Funding bodies had no involvement in the design and conduct of the study; in collection management, analysis and interpretation of the data; or in preparation, review and approval of the paper.

References

1. Pelzer AE, Colleselli D, Bektic J, et al. Clinical and pathological features of screen vs non-screen-detected prostate cancers: is there a difference? *BJU Int.* 2008; 102:24–27. [PubMed: 18341623]
2. Smith DS, Humphrey PA, Catalona WJ. The early detection of prostate carcinoma with prostate specific antigen: the Washington University experience. *Cancer.* 1997; 80:1852–1856. [PubMed: 9351559]
3. Bartsch G, Horninger W, Klocker H, et al. Tyrol prostate cancer demonstration project: early detection, treatment, outcome, incidence and mortality. *BJU Int.* 2008; 101:809–816. [PubMed: 18321314]
4. Loeb S, Roehl KA, Helfand BT, et al. Complications of open radical retropubic prostatectomy in potential candidates for active monitoring. *Urology.* 2008; 72:887–891. [PubMed: 18329080]
5. Makarov DV, Trock BJ, Humphreys EB, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2007. *Urology.* 2005; 69:1095–1101. [PubMed: 17572194]
6. Cuzick J, Fisher G, Kattan MW, et al. Long-term outcome among men with conservatively treated localised prostate cancer. *Br J Cancer.* 2006; 95:1186–1194. [PubMed: 17077805]
7. D'Amico AV, Whittington R, Malkowicz SB, et al. Pretreatment nomogram for prostate-specific antigen recurrence after radical prostatectomy or external-beam radiation therapy for clinically localized prostate cancer. *J Clin Oncol.* 1999; 17:168–172. [PubMed: 10458230]
8. Epstein JI, Walsh PC, Carmichael M, et al. Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. *JAMA.* 1994; 271:368–374. [PubMed: 7506797]
9. Nelson CP, Dunn RL, Wei JT, et al. Contemporary preoperative parameters predict cancer-free survival after radical prostatectomy: a tool to facilitate treatment decisions. *Urol Oncol.* 2003; 21:213–218. [PubMed: 12810209]
10. Freedland SJ, Aronson WJ, Terris MK, et al. Percent of prostate needle biopsy cores with cancer is significant independent predictor of prostate specific antigen recurrence following radical prostatectomy: results from SEARCH database. *J Urol.* 2003; 169:2136–2141. [PubMed: 12771735]
11. Freedland SJ, Aronson WJ, Csathy GS, et al. Comparison of percentage of total prostate needle biopsy tissue with cancer to percentage of cores with cancer for predicting PSA recurrence after radical prostatectomy: results from the SEARCH database. *Urology.* 2003; 61:742–747. [PubMed: 12670558]
12. Goto Y, Ohori M, Arakawa A, et al. Distinguishing clinically important from unimportant prostate cancers before treatment: value of systematic biopsies. *J Urol.* 1996; 156:1059–1063. [PubMed: 8709307]
13. Graefen M, Noldus J, Pichlmeier U, et al. Early prostate-specific antigen relapse after radical retropubic prostatectomy: prediction on the basis of preoperative and postoperative tumor characteristics. *Eur Urol.* 1999; 36:21–30. [PubMed: 10364651]

14. Gretzer MB, Epstein JI, Pound CR, et al. Substratification of stage T1C prostate cancer based on the probability of biochemical recurrence. *Urology*. 2002; 60:1034–1039. [PubMed: 12475665]
15. Epstein JI, Allsbrook WC Jr, Amin MB, et al. The 2005 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma. *Am J Surg Pathol*. 2005; 29:1228–1242. [PubMed: 16096414]
16. Suardi N, Capitanio U, Chun FK, et al. Currently used criteria for active surveillance in men with low-risk prostate cancer: an analysis of pathologic features. *Cancer*. 2008; 113:2068–2072. [PubMed: 18792067]
17. Conti SL, Dall'era M, Fradet V, et al. Pathological outcomes of candidates for active surveillance of prostate cancer. *J Urol*. 2009; 181:1628–1633. discussion 1633–1624. [PubMed: 19233388]
18. Isbarn H, Karakiewicz PI, Ahyai SA, et al. Differences in histopathological and biochemical outcomes in patients with low Gleason score prostate cancer. *BJU International*. 2009; 105:818–823. [PubMed: 19751264]
19. Peller PA, Young DC, Marmaduke DP, et al. Sextant prostate biopsies. A histopathologic correlation with radical prostatectomy specimens. *Cancer*. 1995; 75:530–538. [PubMed: 7529129]
20. Wills ML, Sauvageot J, Partin AW, et al. Ability of sextant biopsies to predict radical prostatectomy stage. *Urology*. 1998; 51:759–764. [PubMed: 9610589]
21. Huland H, Hammerer P, Henke RP, et al. Preoperative prediction of tumor heterogeneity and recurrence after radical prostatectomy for localized prostatic carcinoma with digital rectal, examination prostate specific antigen and the results of 6 systematic biopsies. *J Urol*. 1996; 155:1344–1347. [PubMed: 8632570]
22. Badalament RA, Miller MC, Peller PA, et al. An algorithm for predicting nonorgan confined prostate cancer using the results obtained from sextant core biopsies with prostate specific antigen level. *J Urol*. 1996; 156:1375–1380. [PubMed: 8808875]
23. Tigrani VS, Bhargava V, Shinohara K, et al. Number of positive systematic sextant biopsies predicts surgical margin status at radical prostatectomy. *Urology*. 1999; 54:689–693. [PubMed: 10510929]
24. Ravery V, Chastang C, Toubanc M, et al. Percentage of cancer on biopsy cores accurately predicts extracapsular extension and biochemical relapse after radical prostatectomy for T1–T2 prostate cancer. *Eur Urol*. 2000; 37:449–455. [PubMed: 10765076]
25. Conrad S, Graefen M, Pichlmeier U, et al. Systematic sextant biopsies improve preoperative prediction of pelvic lymph node metastases in patients with clinically localized prostatic carcinoma. *J Urol*. 1998; 159:2023–2029. [PubMed: 9598511]
26. Yoon JH, Chen MH, Renshaw AA, et al. Predictive factor analysis as the basis for the clinical utility of percent positive prostate biopsies in patients with intermediate-risk prostate cancer. *Urology*. 2002; 60:454–457. [PubMed: 12350483]
27. Ravery V, Boccon-Gibod LA, Dauge-Geffroy MC, et al. Systematic biopsies accurately predict extracapsular extension of prostate cancer and persistent/recurrent detectable PSA after radical prostatectomy. *Urology*. 1994; 44:371–376. [PubMed: 7521093]
28. Mortensen MM, Mortensen PS, Borre M. Percentage of tumour-positive biopsy cores: an independent predictor of extraprostatic disease. *Scand J Urol Nephrol*. 2009; 43:109–113. [PubMed: 19242861]
29. Lotan Y, Shariat SF, Khoddami SM, et al. The percent of biopsy cores positive for cancer is a predictor of advanced pathological stage and poor clinical outcomes in patients treated with radical prostatectomy. *J Urol*. 2004; 171:2209–2214. [PubMed: 15126787]
30. Bostwick DG, Qian J, Bergstralh E, et al. Prediction of capsular perforation and seminal vesicle invasion in prostate cancer. *J Urol*. 1996; 155:1361–1367. [PubMed: 8632575]
31. Brimo F, Vollmer RT, Corcos J, et al. Prognostic value of various morphometric measurements of tumour extent in prostate needle core tissue. *Histopathology*. 2008; 53:177–183. [PubMed: 18752501]
32. Harnden P, Shelley MD, Naylor B, et al. Does the extent of carcinoma in prostatic biopsies predict prostate-specific antigen recurrence? A systematic review. *Eur Urol*. 2008; 54:728–739. [PubMed: 18603352]

33. Bismar TA, Lewis JS Jr, Vollmer RT, et al. Multiple measures of carcinoma extent versus perineural invasion in prostate needle biopsy tissue in prediction of pathologic stage in a screening population. *Am J Surg Pathol*. 2003; 27:432–440. [PubMed: 12657927]
34. Briganti A, Chun FK, Hutterer GC, et al. Systematic assessment of the ability of the number and percentage of positive biopsy cores to predict pathologic stage and biochemical recurrence after radical prostatectomy. *Eur Urol*. 2007; 52:733–743. [PubMed: 17350750]
35. D'Amico AV, Whittington R, Malkowicz SB, et al. Clinical utility of the percentage of positive prostate biopsies in defining biochemical outcome after radical prostatectomy for patients with clinically localized prostate cancer. *J Clin Oncol*. 2000; 18:1164–1172. [PubMed: 10715284]
36. D'Amico AV, Whittington R, Malkowicz SB, et al. Combination of the preoperative PSA level, biopsy Gleason score, percentage of positive biopsies, and MRI T-stage to predict early PSA failure in men with clinically localized prostate cancer. *Urology*. 2000; 55:572–577. [PubMed: 10736506]
37. Presti JC Jr, Shinohara K, Bacchetti P, et al. Positive fraction of systematic biopsies predicts risk of relapse after radical prostatectomy. *Urology*. 1998; 52:1079–1084. [PubMed: 9836558]
38. Ploussard G, Xylinas E, Salomon L, et al. The role of biopsy core number in selecting prostate cancer patients for active surveillance. *Eur Urol*. 2009; 56:891–1104. [PubMed: 19683860]
39. Freedland SJ, Terris MK, Csathy GS, et al. Preoperative model for predicting prostate specific antigen recurrence after radical prostatectomy using percent of biopsy tissue with cancer, biopsy Gleason grade and serum prostate specific antigen. *J Urol*. 2004; 171:2215–2220. [PubMed: 15126788]
40. Ravery V, Schmid HP, Toubanc M, et al. Is the percentage of cancer in biopsy cores predictive of extracapsular disease in T1–T2 prostate carcinoma? *Cancer*. 1996; 78:1079–1084. [PubMed: 8780546]
41. Linson PW, Lee AK, Doytchinova T, et al. Percentage of core lengths involved with prostate cancer: does it add to the percentage of positive prostate biopsies in predicting postoperative prostate-specific antigen outcome for men with intermediate-risk prostate cancer? *Urology*. 2002; 59:704–708. [PubMed: 11992844]
42. Okotie OT, Aronson WJ, Wieder JA, et al. Predictors of metastatic disease in men with biochemical failure following radical prostatectomy. *J Urol*. 2004; 171:2260–2264. [PubMed: 15126798]
43. Miyake H, Hara I, Kurahashi T, et al. Clinicopathological features of patients with biochemical recurrence after radical prostatectomy without progressive rise in serum prostate-specific antigen. *Urol Int*. 2006; 77:200–204. [PubMed: 17033205]
44. Taplin ME. Biochemical (prostate-specific antigen) relapse: an oncologist's perspective. *Rev Urol*. 2003; 5(Suppl 3):S3–S13.

Figure 1.

Distribution of cancer-positive cores according to the total number of cores reviewed, in cases diagnosed by needle biopsy ($n=727$)

Figure 2.

Kaplan–Meir plot estimating prostate cancer cause-specific survival according to the extent of cancer in the biopsy: **a** percentage cancer-positive cores $n=727$; percentage length of cancer in the cores, **b** quintiles, **c** 30% cutoff point ($n=737$) for men diagnosed by needle biopsy

Table 1

Measurements of cancer extent made including abbreviations and calculations

Different measurements of cancer extent on prostate core biopsies	Abbreviations and calculations
Total number of cores	TNC
Number of cores with cancer	NCC
Total length of cores	TLC
Length of cancer in all cores	LCC
Percentage of cancerous cores	$PCC = NCC/TNC \times 100$
Percentage length of cancer	$PLC = LCC/TLC \times 100$

Table 2

The added value of pathological assessments of the extent of cancer (PCC, NCC, PLC, LCC) in a multivariate model including Gleason score (G) and baseline PSA level for predicting prostate cancer mortality in men with conservatively treated prostate cancer diagnosed by needle biopsy

Variable	Number	χ^2 (1df) ^h	$\Delta\chi^2$	P value
Positive cores (%)				
G ^a	727	59.8	–	
G + PSA ^b	727	71.3	11.6	<0.001
G + PSA + PCC ^c	727	79.5	8.1	0.004
G + PSA + NCC ^d	727	71.4	0.45	0.50
Length of cancer (%)				
G	737	63	–	
G + PSA	737	73.1	10.1	0.002
G + PSA + PLC quintiles ^e	737	78.7	5.6	0.018
G + PSA + PLC binary ^f	737	79.5	6.4	0.012
G + PSA + LCC ^g	737	74.1	0.96	0.3
Combined model				
G	723	59.7	–	
G + PSA	723	70.5	10.8	0.001
G + PSA + PCC	723	78.3	7.8	0.005
G + PSA + PLC binary	723	75.1	4.5	0.03
G + PSA + PLC quintiles	723	74.7	4.2	0.04
G + PSA + PCC + PLC binary	723	78.8	0.5	0.5

G Gleason score, PSA prostate-specific antigen, PCC percentage of cancer-positive cores, NCC number of cancer-positive cores, PLC percentage length of cancer, PLC percentage length of cancer, LCC length of cancer

^aG score groups: 5, 6, 7, 8, 9

^bPSA (ng/ml) groups: 0–4, >4–10, >10–25, >25–50, >50–100

^cPCC (%) groups: < 50, 50 to <100, 100

^dNCC (1, 2, 3, 4)

^ePLC (%) quintiles: 1.8–14.1, 14.2–29.5, 30–49.5, 50–76, 76.1–100

^fPLC binary: 30, >30, cut off

^gLCC (mm) continuous

^hAll chi-squared values (χ^2) are for trend and are all on one degree of freedom (df)

Table 3

Multivariate analysis of pathological assessments of the extent of cancer measured as PCC, in a model including G and baseline PSA level for predicting prostate cancer mortality in men with conservatively treated prostate cancer diagnosed by needle biopsy ($n=727$)

Variable	N (%)	Hazard ratio (95% CI)	χ^2 (1df) ^a contribution	P value
Gleason score				
<7	262 (36)	1 (ref)	38	<0.0001
7	271 (37)	1.78 (1.17–2.73)		
>7	194 (27)	3.47 (2.26–5.31)		
PSA (ng/ml)				
0–4	52 (7)	1 (ref)	11	0.001
4–10	138 (19)	0.68 (0.35–1.36)		
10–25	261 (36)	0.68 (0.37–1.26)		
25–50	160 (22)	1.5 (0.82–2.75)		
50–100	116 (16)	1.35 (0.72–2.51)		
PCC (%)				
<50	138 (19)	1 (ref)	7	0.008
50 to <100	255 (35)	1.38 (0.82–2.33)		
100	334 (46)	1.74 (1.06–2.85)		

χ^2 chi-squared, *df* degrees of freedom, *CI* confidence interval, *ref* reference category, *PSA* prostate-specific antigen, *PCC* percentage of cancer-positive cores, *PLC* percentage length of cancer in the cores

^a All chi-square values (χ^2) are for trend and are all on one degree of freedom (df)