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ANATOMICAL PATHOLOGY

Macroscopic features of prostate cancer

Claes Lindh[1], Brett Delahunt[2], Lars Egevad[1]

[1]*Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden;* [2]*Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand*

Summary

This study investigates the macroscopic features of prostate cancers in unfixed prostatic tissue.

For the study 514 radical prostatectomy specimens received at the Karolinska University Hospital were examined. The glands were bisected horizontally prior to fixation.

Features on the cut surface of the prostate that were considered conclusive or suspicious for cancer were seen in 52% and 24% of specimens, respectively. In microscopic sections from these areas substantial cancers (≥2 mm) were found in 94% and 69%, of glands, respectively. When no cancer was seen grossly, substantial cancers were still identified histologically in 56% of cases on the cut surface of the prostate. Of substantial tumours 58% had distinct gross findings and 20% were considered to be suspicious for cancer on macroscopic examination. It was noted that gross assessment of the tumour diameter usually underestimated the microscopic extent of the tumour ($p < 0.001$). Of tumours that could be identified conclusively, 30% were tan, 30% white, 16% yellow and 24% orange. Transition zone tumours were most often orange (61%) while peripheral zone tumours were usually tan or white (35% and 33%). All macroscopically identifiable cancers were poorly circumscribed. Among substantial cancers, transition zone tumours were less frequently visualised than peripheral zone tumours (33% and 13%, respectively; $p < 0.001$).

Findings conclusive for cancer macroscopically usually predict microscopic cancer, but substantial cancers may be present even if no cancer is seen grossly. Transition zone tumours are more difficult than peripheral zone tumours to visualise macroscopically.

Key words: Prostatectomy; pathology; prostate cancer; macroscopic; adenocarcinoma.

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INTRODUCTION

Carcinoma of the prostate is one of the leading causes of cancer-related death in the developed world.[1] In view of this it may be assumed that the macroscopic features of this tumour would have been extensively investigated, but the literature on this topic is surprisingly limited. One of the reasons for this paucity of information is that radical surgery was almost never performed before the 1980s and transurethral resection does not provide specimens suitable for the study of gross pathology. Even today radical prostatectomy specimens are usually not dissected for the preparation of histological sections until after formalin fixation. It is recognised that fixation results in distortion of the gland and that this confounds observations regarding the appearance of any tumour present.[2] Occasional reports have been published on the frequency of grossly visible cancers in radical prostatectomy specimens, but these have not included a systematic description of the macroscopic appearance of prostate cancer in an unfixed state.[3,4]

The gross pathology of prostate cancer is not only of interest for descriptive purposes. Several biobanking techniques depend on an ability to identify cancer grossly.[5,6] Although novel molecular techniques have been developed that enable genetic analysis of formalin fixed, paraffin embedded tissues, snap frozen tissue is still often preferred and for this reason accurate identification of tumour position is mandatory.

The aim of this study was to describe the macroscopic features of prostate cancer with emphasis on tumour colour, zonal characteristics and the correlation between gross and microscopic findings. It is anticipated that this will provide information that is helpful both for tumour sampling and for the biobanking of fresh tissue from surgical specimens. The present study is to our knowledge the first detailed report on macroscopic features of prostate cancer in unfixed specimens.

MATERIAL AND METHODS

The study is based upon 514 radical prostatectomy specimens accessioned at the Department of Pathology at the Karolinska University Hospital between 2002 and 2010. Patients had not received pre-operative therapy and in particular those who had undergone preoperative hormone treatment were excluded from the study. Prostatectomy specimens were transported directly from the operation room to the pathology laboratory. All specimens were examined by the same pathologist with a special interest in urological pathology (LE). Upon arrival the prostate glands were measured, weighed and bisected horizontally through the level of any palpable nodules, positive preoperative biopsy sites or the junction of the mid and apical thirds of the gland. A photograph of the gross specimen was taken of the unfixed cut surfaces. Gross findings that were considered conclusive or suspicious for cancer on cut surfaces were noted on a schematic diagram. Findings were classified as conclusive when they were distinctly different from the surrounding benign prostatic tissue by colour and/or texture. A classification of suspicious was given to those cases where the tumour was not markedly different from benign prostatic tissue, e.g., when the difference in colour and/or consistency of the cut surface was subtle.

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Macroscopic findings determined as conclusive for cancer were classified according to colour, being designated as tan, white, yellow or orange, while more subtle changes were recorded as suspicious, without further classification.

After fixation for a minimum of 24 h the surface of the prostate was inked. The gland was sliced horizontally at 4 mm intervals, while the apical and basal slices were cut in the sagittal plane and all tissue was embedded for histological examination. Sections were cut at 4 µm thickness, whole-mounted and stained with haematoxylin and eosin. The seminal vesicles were cut longitudinally and totally embedded. The specimens were examined microscopically with reporting of the histopathological parameters; Gleason score, tumour stage and surgical margin status. The tumour focus that was thought to be most important for patient outcome was considered the index tumour. In most cases this was the largest tumour focus of the specimen, but occasionally a smaller tumour of higher grade was noted as index tumour. The position of the tumour was circumscribed with India ink on the glass slides and the slides were then scanned on a flatbed scanner. The level of the section in relation to the unfixed specimen was noted. The tumour maps were compared with the gross descriptions and agreement was assessed. Tumour foci at the level of inspection were classified as minimal (<2 mm diameter) or substantial (≥2 mm diameter).

In a subset of 54 prostatectomy specimens, macroscopically conclusive cancers were measured in two dimensions in millimeters at gross examination. The tumour dimensions were then measured microscopically in the corresponding histological section and the measures compared.

Statistical analysis

The chi-square test was used to compare differences in proportions. Paired t-tests were used to compare means. A p value of <0.05 was considered to be statistically significant. All tests were undertaken using SPSS software version 23.0.0.0 (SPSS, USA).

Ethical considerations

The study was approved by the Regional Ethics Review Board, Stockholm.

RESULTS

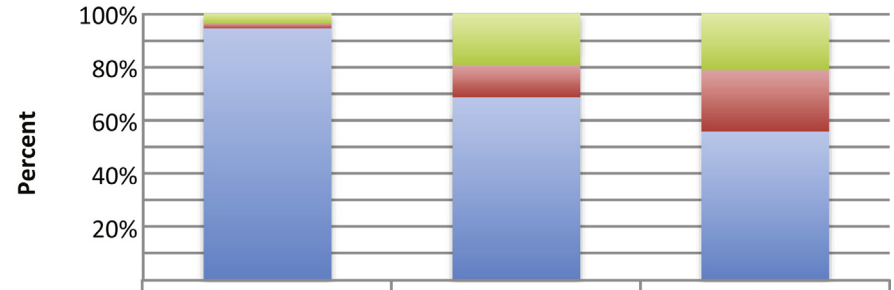
The mean age at the time of surgery for patients in the study was 62.7 years (range 44.2–76.5 years). The mean preoperative serum prostate specific antigen level was 8.8 ng/mL (range 1.1–96 ng/mL). The clinical staging categories were cT1a/b, cT1c, cT2, cT3 and unknown in 9 (1.8%), 275 (53.5%), 180 (35.0%), 16 (3.1%) and 34 (6.6%) cases, respectively. The index tumours within the prostatectomy specimens were in the peripheral zone in 409 (79.6%) cases and in the transition zone in 68 (13.2%) cases. In 37 (7.2%) cases the zonal origin remained unclear due to the large size of the tumour. Extraprostatic extension, positive surgical resection margins and seminal vesical invasion was noted in 215 (41.8%), 154 (30.0%) and 28 (5.4%) cases, respectively. International Society of Urological Pathology (ISUP) grades of the largest tumours within the prostatectomy specimens were grade 1 in 229 (44.6%), grade 2 in 174 (33.9%), grade 3 in 49 (9.5%), grade 4 in 37 (7.2%) and grade 5 in 25 (4.9%) cases.

On gross examination, areas conclusive or suspicious for cancer were seen in 52% (268/514) and 24% (124/514) of cases, respectively, while in 24% (122/514) of specimens no visible pathology was noted. Among cases with conclusive foci of cancer macroscopically, 94% (253/268), 2% (5/268) and 4% (10/268) had microscopically substantial or minimal cancers, or no cancer, respectively, in the corresponding histological section. Among cases with macroscopically suspicious foci 69% (85/124), 12% (15/124) and 19% (24/124) had substantial or minimal cancers or no cancer, respectively, in the corresponding histological section (Fig. 1).

In sections taken from the level of the cut surface examined macroscopically, substantial cancers were found anywhere on the cut surface in 84% (435/514) and minimal cancers in 10% (49/514) of cases, while only 6% (30/514) were free from cancer at the examined level. Peripheral zone and transition zone tumours of substantial size had findings conclusive for cancer at gross examination in 63% (199/316) and 39% (31/79) of cases, respectively ($p < 0.001$) and were not visualised in 13% (42/316) and 33% (26/79) of cases, respectively ($p < 0.001$) (Fig. 2 and 3).

Of the histologically proven substantial tumours, 58% (253/435) had distinctive macroscopic features. Of these 30% were tan (75/253), 30% were white (77/253), 16% were yellow (40/253) and 24% were orange (61/253), while 20% (85/435) were grossly judged as suspicious for cancer (Fig. 4). The positive predictive value for substantial cancer of tan, white, yellow and orange colour at macroscopic examination was 94% (75/80), 96% (77/80), 91% (40/44), 95% (61/64), respectively.

The macroscopic appearance of histological substantial cancers in the peripheral zone was tan in 35% (70/199) (Fig. 5), white in 33% (65/199) (Fig. 6), yellow in 14% (28/199) (Fig. 7) and orange in 18% (36/199) of cases. This compared with the macroscopic appearance of substantial transition zone cancers of which 7% (2/31) were tan, 13% (4/31) were white, 19% (6/31) were yellow and 61% (19/31) were orange (Fig. 8). In cancers where the anatomical zone



	Conclusive	Suspicious	Invisible
No cancer	3.7%	19.4%	21.3%
<2 mm	1.9%	12.1%	23.0%
≥2 mm	94.4%	68.5%	55.7%

Fig. 1 Distribution of microscopic cancer in cases with macroscopic findings conclusive or suspicious for cancer or no visible tumour.