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Platinum Opinion

Current Histopathologic and Molecular Characterisations of Prostate Cancer: Towards Individualised Prognosis and Therapies

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Radical prostatectomy (RP) is a common treatment for prostate cancer (PCa) [1]. The surgical specimen plays an important role in disease annotation and the prediction of future events. Its evaluation should include a definition of morphologic characteristics with prognostic and therapeutic value and a personalised pathology report based on the latest international guidelines. The morphologic evaluation should correlate with and explain pre- and intraoperative findings (Fig. 1A and 1B). Advances in molecular biology mean there will soon be a need to match histopathologic findings with molecular features that could improve prognostication and individualise treatment [2].

This editorial updates the contemporary role of the uropathologist in the era of personalised medicine in the evaluation of the morphologic and molecular characteristics of PCa and their clinical significance.

1. The uropathologist in the personalised medicine era

The macroscopic evaluation of RP specimens should include quality indicators of the surgical procedure, such as specimen integrity, including missing parts, and should take into account the type of surgical procedures, such as nerve sparing and the approach used (open vs minimally invasive). The uropathologist should also consider the effects of previous treatment and/or surgical procedures, such as transurethral resection of the prostate or radiation therapy/focal therapy, and the presence of tissue other than prostate (ie, rectal wall).

Microscopic evaluation, based on the latest international guidelines, should include (1) tumour multifocality, the index tumour, and tumour extent; (2) histopathologic type; (3) Gleason score and grade grouping; and (4) TNM stage including surgical margin status and lymphovascular invasion (LVI).

1.1. Tumour multifocality, index tumour, and tumour volume

Although PCa is usually multifocal (Fig. 1B), the index lesion (mostly defined as the largest tumour) is considered crucial in driving outcomes. Gleason grade, tumour volume, and stage are mostly determined by the index lesion because secondary foci are usually small well-differentiated lesions. Recording tumour volume using a quantitative estimate is recommended, although most studies demonstrating this measure do not provide independent prognostic information beyond standard pathologic parameters [3–5]. Recent data suggest multiparametric magnetic resonance imaging performs well at predicting pathologic features of the index lesion (Fig. 1A), regardless of tumour multifocality [6]. Ahmed et al recently reported a single-centre prospective study in which 56 patients with multifocal PCa were treated only for the largest and highest grade tumour (index tumour).

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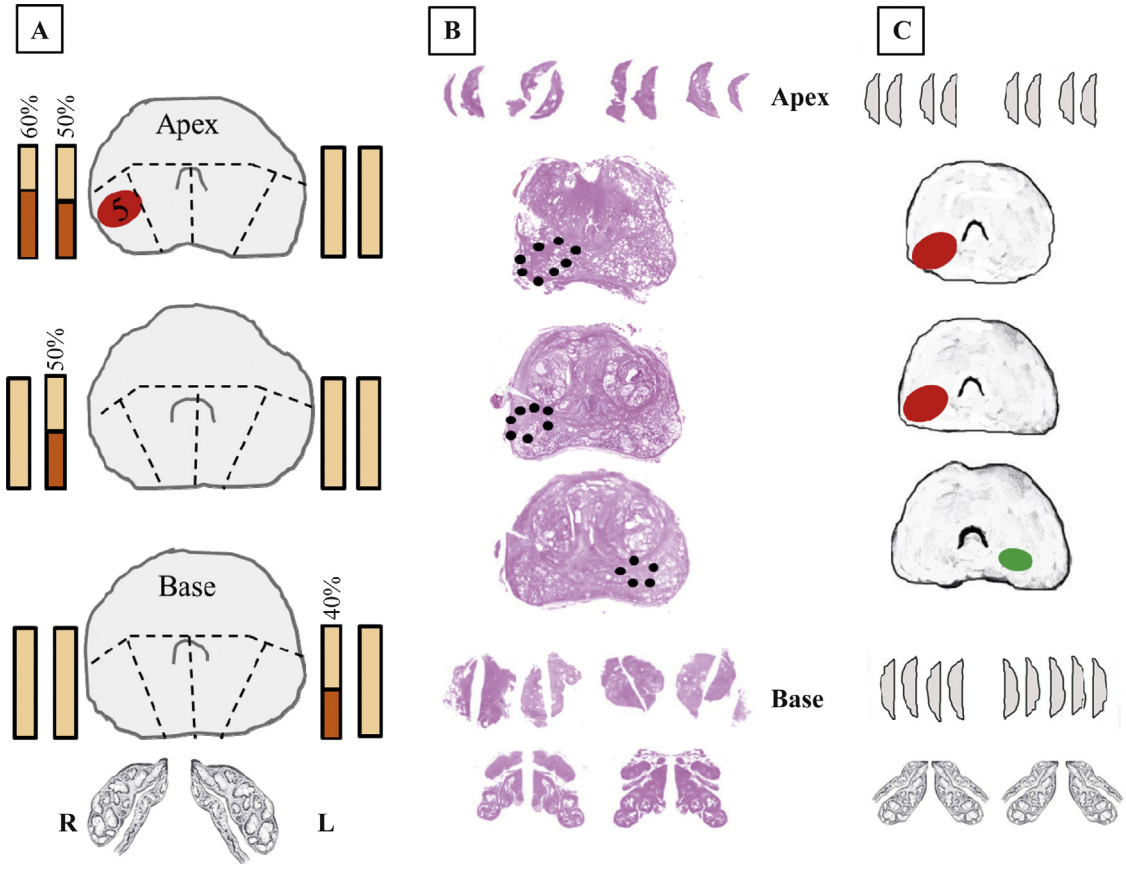

Fig. 1 – (A) The vertical bars represent the biopsy cores and their locations in relation to the prostate drawing in the background. The bars in orange represent the positive cores (ie, biopsies with cancer) including the extension of cancer. The prostate in the background is subdivided into zones according to the guidelines of multiparametric magnetic resonance imaging (mpMRI) evaluation. The red area with the number 5 inside represents an area identified as "Clinically significant cancer is highly likely to be present" (Prostate Imaging Reporting and Data System [PI-RAD] score 5). A combination of bars with an indication of cancer-positive cores, including the extent, and a drawing of the prostate with the results of an mpMRI evaluation, when available, is what should be sent to clinicians. (B) Radical prostatectomy specimen processed with the whole-mount technique. The dotted areas represent the location of the cancer foci. There are two cancer foci. The index nodule (dominant nodule) is present in the body of the prostate, right side, in two consecutive whole-mount sections. It shows the features of a significant cancer (Gleason score 3 + 4 = 7; volume: 0.9 ml). It corresponds to the mpMRI area identified as PI-RAD score 5 in (A). The additional nodule is in the opposite side of the prostate; it is present in one whole-mount section only and shows the features of an insignificant cancer (Gleason score 3 + 3 = 6; volume: 0.4 ml). (C) Prostate map graphically representing the whole mount sections and the location of the two tumour foci, one already identified by mpMRI and both detected with the prostate biopsies and characterised histologically. The tumour focus in red corresponds to the significant cancer (index tumour) and the green to the insignificant cancer. Such a prostate map is sent to clinicians together with the pathology report that includes the macroscopic and microscopic evaluations as well as a summary of the analysis, as seen in Table 1.
L = left side of the prostate gland; R = right side of prostate gland.

Index lesion ablation was associated with little toxicity, and >80% of patients were without clinically significant cancer at 12 mo [7].

The index lesion can be hard to define, and so studies are under way to examine their genetics and thus better define each lesion. Further advances in molecular studies may define or redefine the index tumour as the most aggressive biologically, rather than the largest or most poorly differentiated [8]. Although recording tumour volume using some quantitative estimate is recommended, tumour volume does not provide independent prognostic information once other standard pathologic parameters are known.

Lindberg et al [9], by searching for metastatic-specific DNA alterations in several regions of the prostate, identified the area that gave rise to metastases. The metastasising component probably originated from prostatic ducts via an invasive component with Gleason score 4 + 4 = 8 highly related to the intraductal carcinoma component although located at some distance. Such a finding supports the fact that intraductal carcinoma is a morphologic marker of aggressive disease and a major step forward on the origin of PCa and on the mechanisms of metastatic spread [10].

1.2. Histopathologic type

More than 95% of all prostate carcinomas are referred to as acinar, microacinar, usual, or conventional type. Several variants of PCa have been described including neuroendocrine differentiation, ductal, mucinous, signet ring cell–like, sarcomatoid carcinoma, adenosquamous, and other cancers (some deceptively benign looking). Although relatively uncommon, these variants have prognostic and therapeutic importance. A novel morphologic classification of PCa with neuroendocrine differentiation (NE) was recently published