

Margin status (Required and Recommended)

Reason/Evidentiary Support

A positive surgical margin (PSM) significantly reduces the likelihood of progression-free survival, including prostate-specific antigen (PSA) recurrence-free survival, local recurrence-free survival and development of metastases after radical prostatectomy in multivariate analysis.¹⁻⁶ Moreover, positive margins are associated with a 2.6-fold increased risk of prostate cancer specific mortality.⁷ Careful inking of the outer surface of the radical prostatectomy specimen before macroscopic dissection (grossing) greatly facilitates the determination of margin status. A PSM can then be defined as cancer extending to the inked surface of the specimen, representing a site where the urologist has cut through cancer.^{1,8} PSMs are reported in between 10–48% of patients treated by radical prostatectomy for both organ confined and non-organ confined prostate cancer with the rates in the lower range typically found in more modern cohorts.^{6,9-11}

The presence of prostate carcinoma close to, but not touching the inked margin should not be labelled as a PSM as this finding has been shown to have little, if any, prognostic significance.¹²⁻¹⁴ Close surgical margins are most commonly seen posterolaterally in cases where neurovascular bundle preservation leaves virtually no extraprostatic tissue. Studies on such nerve sparing cases have shown that additional tissue removed from these sites did not contain any carcinoma and a close margin was not associated with a worse prognosis.^{12,14}

Stating the location of the PSM is useful information for the urologist who can then modify future operations to avoid iatrogenic margin positivity and increase the likelihood of curative surgery. The site of the PSM and the number of positive margins have been shown to influence biochemical recurrence and risk of progression. For instance, a margin involving the bladder neck or the posterolateral surface of the prostate has a more significant adverse impact on prognosis than an involved apical or anterior margin.^{11,15}

Type of margin positivity

Intraprostatic margin involvement or capsular incision (CI) occurs when the urologist inadvertently develops the resection margin within the plane of the prostate rather than outside the capsule. CI with a positive surgical margin is diagnosed when malignant glands are cut across adjacent to benign prostatic glands.¹⁶ In these cases, the edge of the prostate in this region is left in the patient. Data on the prognostic significance of CI vary among studies.¹⁷⁻¹⁹ According to the largest series published, a significantly higher recurrence rate is found in patients with CI/intraprostatic margin involvement than in patients with organ confined disease with negative margins, or focal extraprostatic extension (EPE) with negative margins, although CI has a significantly better outcome than that associated with non-focal EPE and positive margins.²⁰

Margin involvement associated with EPE is diagnosed when malignant glands in extraprostatic tissue are transected by the resection margin. This can be difficult to distinguish from capsular incision in some cases, particularly posteriorly and posterolaterally if there is a desmoplastic reaction. Cancer extending to a margin which is beyond the normal contour of the prostate gland, or beyond the compressed fibromuscular prostatic stroma at the outer edge of the prostate, can be diagnosed as a positive surgical margin with EPE, similarly to margin involvement when there is cancer in adipose tissue.¹⁸ At the apex, the histological boundaries of the prostate gland can be difficult to define and

again EPE with a positive margin can be difficult to differentiate from CI/intraprostatic margin involvement. Hence, if carcinoma extends to an inked margin at the apex where benign glands are not transected, this is considered a positive margin in an area of EPE by some authors.^{1,18} In contrast, other authors, and the majority of survey participants at the 2009 International Society of Urological Pathology (ISUP) Consensus Conference, believe there is no reliable method to diagnose EPE in sections from the prostatic apex.²¹

Extent (total) of margin involvement

Although a positive surgical marginal (PSM) has a significant adverse impact on the overall likelihood of progression-free survival, in most published series only about a third of individual patients with a PSM will experience biochemical recurrence.^{2,3,9,22} The expert panel considered that there is sufficient evidence to include measurement of the length of margin involved by carcinoma as an element in the International on Cancer Reporting (ICCR) dataset.^{12,14,20,22-26} In particular, the 5 year prostate-specific antigen (PSA) recurrence risk appears to be significantly greater when the length of the involved margin is 3 mm or more, (53% versus 14%).^{20,23,27-29} However, in one series, Cao et al²⁵ found that the linear length of a positive margin was an independent prognostic factor for organ confined tumours only, i.e. pT2 not pT3, while, another investigation found that the impact of a positive surgical margin after radical prostatectomy was greater in intermediate and high risk groups (based on Gleason score and pre-biopsy PSA) than in low risk patients.⁵ Further studies of such factors potentially affecting the impact of PSMs are required before there is sufficient evidence justifying their inclusion as required (core) data elements. The optimal method of assessing the extent of margin involvement when multiple positive margins are present is currently uncertain, but, until more evidence is available, it is suggested that extent is measured as the linear cumulative length of all positive margins.³⁰

Gleason pattern at the margin

Four recently published papers have found that Gleason pattern/grade or score of the tumour at the positive surgical margin is an independent predictor of biochemical recurrence and may aid optimal selection of patients for adjuvant therapy.^{22,31-33} In one of these studies patients with Gleason pattern 4 or 5 carcinoma (Gleason score 3+4, 4+3, 4+4 or 4+5) at a PSM had double the risk of PSA relapse compared to those with only Gleason grade 3 (score 3+3) at the margin. Moreover, men with Gleason pattern/grade 3 at the PSM had a similar 5-year biochemical relapse-free survival rate to those with negative margins.²² Another study, restricted to men with dominant nodule Gleason score 7 and non-focal EPE, also found that the grade of cancer at the site of a PSM was associated with biochemical recurrence.³¹ The largest series, including 405 cases with a PSM, confirmed that a lower Gleason score at the margin was independently associated with a decreased risk of early biochemical recurrence.³³

In each of the published studies, the potential problem of cautery/thermal artefact was considered - each group noted that in slides where the cancer at the margin was distorted by cautery/thermal or crush artifact and could not be reliably assessed, the margin pattern, or score, was designated as that of the closest, well preserved carcinoma in direct continuity with the distorted neoplastic glands.^{22,31-33} Limiting assessment to only the highest pattern present at the PSM may simplify measurement of this parameter, however, it should be noted that in most of the published studies Gleason score could be reported.³¹⁻³³ In the event there are multiple positive margins with differently scored cancers present, the highest pattern or score should be recorded.

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