Margin status

Reason/Evidentiary Support:

A positive surgical margin (PSM) significantly reduces the likelihood of progression-free survival, including PSA recurrence-free survival, local recurrence-free survival and development of metastases after radical prostatectomy in multivariate analysis.\textsuperscript{1-6} Moreover, positive margins are associated with a 2.6-fold increased risk of prostate cancer specific mortality.\textsuperscript{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\textsuperscript{1,8} (See Fig. 5 below). 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{12,14}

![Figure 5. Positive surgical margin (PSM). Prostatic adenocarcinoma extending to black inked margin (top)](image)

**Extent (total) of margin involvement**

Extent is measured as the linear cumulative length of all positive margins.\textsuperscript{15}

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.\textsuperscript{2-3,9,16} Studies aiming to better quantify the risk associated with a PSM have focussed on a number of factors such as number, location and extent of positive margins. However, the published data relating to these parameters are somewhat contradictory, and the expert panel considered that there is only sufficient evidence to include measurement of the length of margin involved by carcinoma as an element in the ICCR dataset at present.\textsuperscript{12,14,16-21} In particular, the 5 year PSA recurrence risk appears to be significantly greater when the length of the involved margin is 3mm or more, (53% versus 14%).\textsuperscript{17,19} However, in one series, Cao et al\textsuperscript{20} 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.\textsuperscript{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.
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.22 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.23-25 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 EPE with negative margins, although CI has a significantly better outcome than that associated with nonfocal EPE and positive margins.19

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.24 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.1,24 In contrast, other authors, and the majority of survey participants at the 2009 ISUP Consensus Conference, believe there is no reliable method to diagnose EPE in sections from the prostatic apex.26

Gleason score at the margin

Following review of feedback on the draft prostate cancer (radical prostatectomy) dataset and commentary, the expert panel has included the Gleason score of the tumour at the positive surgical margin as a recommended (non-core) element of the ICCR dataset. Three recently published papers have found that Gleason score or grade 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.16,27-28 In one of these studies patients with Gleason grade 4 or 5 carcinoma (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 score 3 at the PSM had a similar 5-year biochemical relapse-free survival rate to those with negative margins.16 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.27

In the event there are multiple positive margins with differently scored cancers present, the highest score should be recorded.

References


