

GLOSSARY

PSA

Prostate-specific antigen

ROC

Receiver operating characteristic: a statistical validation tool used to measure how well logistic regression models have predicted a particular binary outcome. The area under the curve (AUC) equates to the probability of being able to discriminate between the two possible outcomes, with the ideal value being 1.0

3D-CRT

Three-dimensional conformal radiation therapy

Predicting clinical outcome in prostate cancer

Improved diagnostic methods are urgently needed in order to avoid the unnecessary treatment of men with clinically indolent prostate cancer. Kreisberg and colleagues have previously demonstrated increased phosphorylation (activation) of the protein kinase Akt, as well as decreased phosphorylation (inactivation) of extracellular signal-regulated kinase (ERK), in high-Gleason-grade prostate tumors. This prompted them to investigate whether these biomarkers can be used to predict clinical outcome.

Prostate tumors were stained immunohistochemically for phosphorylated Akt (pAkt) and phosphorylated ERK (pERK). Degree of staining, measured on a scale of 0–300, was compared between tumors from cases of PSA failure (detectable and rising PSA; a surrogate for ‘poor’ outcome) and non-failure (undetectable PSA 5 years after prostatectomy; a surrogate for ‘good’ outcome).

pAkt staining was significantly stronger in the 37 PSA failures than in the 16 non-failures (222.18 ± 33.9 vs 108.79 ± 104.57 ; $P < 0.001$). In contrast, pERK staining was weaker in the PSA failures than in the non-failures, although this difference was not statistically significant. The area under the ROC curve for pAkt and pERK predicting PSA failure was 0.84, indicating very good discrimination. Gleason score at prostatectomy was not predictive of PSA failure in this study, even though Gleason grading is commonly used to predict clinical outcome.

The authors conclude that increased pAkt, with or without decreased pERK, is highly predictive of PSA failure in prostate cancer patients, and so warrants further investigation as a useful biomarker of clinically aggressive disease.

Original article Kreisberg JI *et al.* (2004) Phosphorylation of Akt (Ser⁴⁷³) is an excellent predictor of poor clinical outcome in prostate cancer. *Cancer Research* **64**: 5232–5236

Reducing rectal toxicity in 3D-CRT

3D-CRT aims to increase radiation dose to the target tissue in prostate cancer, but this approach has been associated with a moderate increase in late rectal bleeding. Zapatero

et al. have investigated the clinical and dosimetric factors predicting this complication.

Records were retrospectively analyzed for 107 patients with Stage T1c–T3 prostate cancer who had been treated with 3D-CRT. Dose levels were 70.0 Gy ($n=21$), 72.0 Gy ($n=57$) and 75.6 Gy ($n=29$). The primary endpoint was Grade 2 or worse rectal bleeding. Late bleeding was defined as bleeding occurring >120 days after the end of treatment.

The 4-year actuarial incidence of Grade 2 or worse late rectal bleeding was $7.7\% \pm 2.5\%$. Rectal volume was significantly lower and mean dose to the rectal volume (D_{mean}) was significantly higher in patients with rectal bleeding than in those without (median rectal volume 49 cm^3 vs 85 cm^3 , $P < 0.024$; D_{mean} 57.0 Gy vs 46.0 Gy , $P < 0.0005$). The percentage of rectum receiving >60.0 Gy (Vr_{60}) also correlated with rectal bleeding ($P < 0.0005$). ROC curve analysis confirmed Vr_{60} and rectal D_{mean} as good predictors of late rectal bleeding: the area under the curve was 0.889 and 0.892, respectively.

While data from larger, prospective studies are awaited, the authors have applied new constraints at their center (rectal D_{mean} 50.0 Gy and Vr_{60} 42%) as a result of this study.

Original article Zapatero A *et al.* (2004) Impact of mean rectal dose on late rectal bleeding after conformal radiotherapy for prostate cancer: Dose-volume effect. *Int J Radiat Oncol Biol Phys* **59**: 1343–1351

Improving continence following radical prostatectomy

Urinary incontinence is a major side effect of radical prostatectomy. In an effort to improve postoperative continence, van Randenborgh and colleagues have instituted a procedure in which a longer intraprostatic urethral stump is created for vesicourethral anastomosis. They have recently performed a retrospective study comparing this approach with an earlier technique.

A total of 1,013 patients underwent radical retropubic prostatectomy for localized prostate cancer. In patients operated on between 1986 and 1996 (group 1, $n=610$), the urethra was transected at the apex, whereas those treated between 1997 and 2002 (group 2, $n=403$) were subjected to the new procedure. Postoperative continence status was compared between the