GLOSSARY

RECEIVER OPERATING CHARACTERISTIC CURVE
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 null value represented by 0.5, and the ideal value being 1.0

GLEASON SUM
Sum of grades assigned to the two largest cancerous areas of tissue samples; grades range from 1 (least aggressive) to 5 (most aggressive)

Postoperative prognostic prediction models for nonmetastatic RCC

Most patients with nonmetastatic renal cell carcinoma undergo nephrectomy, but predicting long-term survival can be difficult. Although several prognostic models exist, few have been validated and it was unknown how well they could be generalized to all patients with nonmetastatic renal cancer undergoing this surgery. This retrospective study aimed to compare several prognostic models directly, with overall survival as the primary endpoint; secondary endpoints were cancer-specific and recurrence-free survival.

Of the four models selected, those designed by Yaycioglu *et al.* and Cindolo *et al*. assign preoperative prognostic scores; the other two, the University of California at Los Angeles integrated staging system (UISS) and the model developed by Kattan *et al*., assign postoperative scores. The authors applied each model to data collected from 2,404 patients who had undergone surgery for renal cell carcinoma in six European clinics between 1984 and 2002. Clinical and pathologic information was gathered from databases compiled in each clinic and information about outcome was collected by phone call or by contacting patients' primary-care doctors or relatives. Each model's predictive ability was calculated using a RECEIVER OPERATING CHARACTERISTIC CURVE.

Although all four models discriminated prognosis well, the Kattan model was the most accurate (with a value of 0.706, where 1.0 is ideal), closely followed by the UISS. Having applied the models to a heterogeneous group of patients across three European countries, the authors suggest their results will help clinicians to predict outcome, although they hope that current models will be supplemented by molecular prognostic markers as technology develops.

Rebecca Doherty

Original article Cindolo L *et al.* (2005) Comparison of predictive accuracy of four prognostic models for nonmetastatic renal cell carcinoma after nephrectomy. A multicenter European study. *Cancer* **104:** 1362–1371

A new therapeutic approach in erectile dysfunction

Despite the popularity of sildenafil and other phosphodiesterase-5 (PDE5) inhibitors for the treatment of erectile dysfunction, these drugs show little benefit in about a third of patients. In addition, some patients experience adverse effects such as headache and facial flushing. In an attempt to find a superior treatment, Lin and colleagues have explored the idea of using small interfering RNA (siRNA) to suppress PDE5 expression at the mRNA level.

The researchers selected a 19-base region of human PDE5 cDNA thought to be identical in the rat. They incorporated this sequence into a double-stranded, 64-base oligonucleotide and cloned this into a vector to produce the 'pPDE5-silencer' construct. They then demonstrated that rat and human cavernous smooth-muscle cells transfected with this construct produced lower levels of PDE5 than those transfected with 'empty' vector. This was accompanied by prolonged cGMP accumulation in the treated cells.

Next, they transferred the siRNA-expressing cassette to a lentiviral vector and injected this into the penises of nine Sprague-Dawley rats. Cavernous nerve electrostimulation tests 3 months later showed that the siRNA-treated rats had enhanced erectile function compared with nine rats treated with vector alone. This finding was reinforced by immunohistochemical staining experiments, which showed lower PDE5 levels in the cavernous smooth muscle of the treated animals.

In summary, these studies demonstrate that a PDE5 siRNA method can decrease PDE5 expression and improve erectile function in rats. A new therapy for erectile dysfunction based on this technique appears promising.

Ruth Kirby

Original article Lin G *et al.* (2005) Improving erectile function by silencing phosphodiesterase-5. *J Urol* **174:** 1142–1148

Tumor multifocality is associated with worse outcome in prostate cancer

Tumor grade is one of the most important prognostic factors for prostate cancer. Although the GLEASON SUM considers only the two largest (primary and secondary) neoplastic areas in the assessment of tumor grade, additional (tertiary) neoplasms can occur. Previous studies suggested that the presence of a tertiary neoplasm was associated with