

Mini-reviews

There are four mini-reviews in this section, with a very strong emphasis on urological oncology; two on prostate cancer and two on renal cancer. The spread of countries from which they came reflects the international authorship of contributors to the Journal: the UK, Canada, USA and Germany respectively.

Radical prostatectomy with positive surgical margins: how are patients managed?

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INTRODUCTION

The last decade has seen a trend towards organ-confined prostate cancer, primarily due to the widespread use of PSA testing [1]. As a result, local treatment options such as brachytherapy, cryotherapy, radiotherapy and radical prostatectomy (RP) are used increasingly. The aim of RP is to completely excise the prostate, with clear margins. However, despite the availability of pretreatment staging and predictive nomograms, ≈40% of patients will have biochemical failure after RP, and up to a third of these men will develop metastatic disease and die from prostate cancer. Positive surgical margins (PSMs) suggest residual disease and carry a greater risk of PSA progression, as well as local and systemic spread [2,3]. The PSA test-induced stage shift towards smaller, organ-confined tumours, along with improving surgical techniques, has resulted in a reduction in PSM rates over the last two decades. However, present PSM rates are still significant, with various series reporting rates of 5–60% [4,5].

PSM

Previous definitions for a PSM have included tumour within 1 mm of the margin, or at the apex as tumour in the distal 5 mm of the prostate. Prostate tumours often extend close to the edge of the gland. Epstein and Sauvegeot [6] assessed the proximity of tumour to the surgical margin and concluded that recurrence rates were similar whether tumour cells approached or were safely distant from the inked surface. A 'close' margin therefore does not seem to matter, and most pathologists now define a PSM as the presence of neoplastic cells in contact with the ink on the margin.

Differing PSM rates in previous studies were attributed to tumour stage, surgical technique and differences in specimen processing. Table 1 [7–9] and Table 2 [4,5,10–14] show distributions of PSMs based on the clinical stage of prostate cancer and the surgical approach used in RP. Such variable rates of PSMs for all clinical stages may depend on the surgical awareness and approach during RP. There are also no significant differences in PSM rates amongst both laparoscopic and open techniques for RP, as shown from these studies. However, such contrasting rates among studies might be explained by either differences in patient populations or surgical expertise. The choices

of histological preparation (whole-mount, 2–3 mm or 3–4 mm sections) are also known to affect the rate of PSMs in prostatectomy specimens [15]. Hall *et al.* [16] observed that 4–6 mm sections would miss up to 12% of the PSMs identified on 2–3 mm sections. Furthermore, compared to complete examination of the specimen, histological assessment of only the area of carcinoma would miss an estimated 16% of PSMs. A PSM in surgical specimens may be due to the growth of tumour towards the edge of the prostate, incision into the prostate (capsular incision) or transection of extracapsular tumour.

Although the risk of biochemical recurrence is increased with PSMs, the TNM staging classification for prostate cancer does not equate PSMs to a higher stage. Specimens with PSMs in the absence of extracapsular extension are designated as pT2 disease. Staging may also be complicated because the prostatic capsule at the apex is poorly defined, so it is unclear if an apical PSM involves tumour within or outside the boundaries of the capsule.

PSM: STRATIFYING THE RISK

After RP a PSM conveys a greater risk of biochemical progression. D'Amico *et al.* [17] found that the 2-year PSA failure rates after RP were 45–55% in patients with PSMs, compared to 15–25% in those with organ-confined disease. Several factors have been assessed to see if it is possible to further stratify the risk of disease recurrence in patients with PSMs.

Multiple PSMs have been shown to carry a worse prognosis in virtually all studies. Sofer *et al.* [18], after a multivariate analysis on the number of PSMs (solitary vs multiple) showed that there was a statistically significantly greater risk of recurrence in patients with more than one PSM, with a hazard ratio of 2.19 at the 95% CI. A similar result was reported by Obek *et al.* [19], who showed that at a mean follow-up of 25 months, the recurrence rate in patients with multiple PSMs was 43%, vs 24% in those with a single focus. Furthermore, patients with two or more PSMs were 2.5 times more likely to have a shorter time to recurrence. It was also shown that an extensive PSM carries a greater risk of progression than a focal area.

TABLE 1 Effects of clinical stage on PSM rates

Reference	Group/clinical stage	PSM rate, %
Clinical stage Freedland <i>et al.</i> [7]	Overall	23.1
	T1/2/3	28.1/22.4/50.0
Wieder <i>et al.</i> [8]	Overall	28
	T1a/T1b/T1c/T2a/T2b/T2c/T3a	5/22/23/17/36/27/40
Hull <i>et al.</i> [9]	Overall	12.8
	T1a/T1b/T1c/T2a/T2b/T2c	0/28.8/11.6/7.5/14.5/17.2

Reference	Surgical approach and group	PSM rate, %	TABLE 2 Effects of surgical approaches on PSMs
Palisaar <i>et al.</i> [4]	Retropubic		
	pT2 nerve-sparing	6.5	
Ward <i>et al.</i> [10]	pT2 not nerve sparing	5.1	
	Retropubic:		
Korman <i>et al.</i> [11]	wide local excision	42	
	nerve sparing	34	
Boccon-Gibod <i>et al.</i> [5]	Perineal	16	
	Retropubic	22	
Erdogru <i>et al.</i> [12]	Rates for for T1 and T2:		
	perineal	56	
Brown <i>et al.</i> [13]	retropubic	61	
	Extraperitoneal	22.6	
Salomon <i>et al.</i> [14]	Transperitoneal laparoscopic	20.7	
	Laparoscopic	16.9	
Salomon <i>et al.</i> [14]	Retropubic	20.0	
	PSA < 10 ng/mL:		
	retropubic	20.9	
	perineal	18.4	
	laparoscopic	20.6	

The incidence of PSMs is highest in the apical region, approaching 64% of all PSMs. Improved surgical technique and a better understanding of the venous anatomy have reduced the difficulties related to bleeding in the confined space of the male pelvis, but the short inferior pedicle of the prostate (through which the tumour may have extended), and attempts to preserve continence by dividing the urethra close to the apex, risks an apical PSM. Salomon *et al.* [20] compared PSM locations in patients undergoing RP based on the surgical approach. The distribution for the retropubic, perineal and laparoscopic surgical approaches was 50%, 33% and 44% for apical margins, 29%, 42% and 14% involving the bladder neck and 21%, 25% and 42% involving the posterolateral wall, respectively. These findings suggest that the PSM location may vary depending on the surgical approach used in RP.

The impact of margin location on disease progression is not clear. Table 3 [19,21–23] outlines a few recent studies based on PSM location. Contrary to some studies Epstein *et al.* [21] showed that patients with apical PSMs progressed more often those with negative margins. Obek *et al.* [19] and Blute *et al.* [23] instead concluded that when comparing different anatomical foci, the bladder neck region carried the highest risk of disease progression.

CAPSULAR INCISION

Poor surgical technique and the close anatomical proximity of the prostate to neighbouring pelvic structures increase the risk of capsular incision of the prostate. Although not well defined, incision through the apex probably occurs due to insufficient

TABLE 3 Effect of PSM location on recurrence rate

Reference	Findings
Obek <i>et al.</i> [19]	Recurrence rate for bladder neck PSM associated with greatest risk of disease recurrence. Second most important site is a posterolateral PSM, associated with 48% recurrence rate
Epstein <i>et al.</i> [21]	Recurrence rate for apical PSMs higher than for negative margins
Grossfeld <i>et al.</i> [22]	Recurrence rate for apical PSMs no different from other PSM locations
Blute <i>et al.</i> [23]	Recurrence rate for bladder neck PSMs; significantly worse disease-free survival than other PSM locations

mobilization of the distal prostate. Shuford *et al.* [24] concluded that patients with capsular incision-related PSMs have similar biochemical recurrence rates to those with pT3a disease and PSMs, although previous studies suggest a lower risk.

EXTRACAPSULAR EXTENSION

Blute *et al.* [23] also found that men with PSMs and no extracapsular spread had a lower rate of recurrence than men with extracapsular disease. This was contradicted by the SEARCH database study group [7], who found that men with PSMs and no extracapsular spread had a similar recurrence risk to those with extracapsular disease (regardless of margin status). Furthermore, Ohori *et al.* [25] reported that apical PSMs were associated with higher rates of seminal vesicle and lymph node involvement, and increased the risk of extraprostatic spread.

REDUCING PSM RATES

Surgical technique is known to affect PSM rates; there is considerable variation in rates among different surgeons. One study showed that although experienced surgeons tend to have lower PSM rates, these varied from 10% to close to 50% even for high-volume surgeons doing similar numbers of RP.

Although it was suggested that the reduction in PSM rates over the last 20 years is due to stage migration and improved patient selection, rather than improved surgical technique, numerous technical modifications have been described to reduce PSM rates. These are usually reported after single-surgeon (or -institution) observational studies, so it is difficult to assess their usefulness. Careful dissection of the prostatic apex is thought to be important and recent

reports have advocated mobilising the prostate before dividing the urethra. This can be done using an antegrade technique, or by dividing the lateral prostatic fascia and mobilising the gland off the rectum before apical dissection. More recently, Walsh *et al.* [26] pioneered the use of video documentation to improve the surgical technique in RP. In that study it was concluded that subtle variations of technique amongst different surgeons could be identified and changes advocated to improve surgical outcome for future patients. Touijer *et al.* [27] used intraoperative video documentation to improve PSM rates in patients undergoing laparoscopic RP. When the 12 patients with PSMs were reviewed, video analysis concluded that eight were due to technical error. Intraoperative filming has also helped to improve PSM rates after robotic RP using the da Vinci system (Intuitive Surgical, Sunnyvale, CA, USA) [28]. In one study, videotape from 50 procedures was reviewed and technical alterations made, resulting in a reduction in PSM rates from 36% to 17% in patients with pT2 tumours.

Although overall PSM and biochemical recurrence rates are similar for perineal and retropubic RP procedures, the perineal approach carries a higher risk of capsular incision and a surgically induced PSM. Bladder-neck sparing does not increase PSM rates, although it does seem to reduce the magnitude of the surgical margin. Similarly, nerve-sparing RP does not appear to worsen PSM or biochemical recurrence rates in well-selected patients. As well as considering preoperative risk factors, careful visual and tactile assessment of the neurovascular bundle is important in determining the suitability of a nerve-sparing procedure. Laparoscopic RP provides better magnification for visual assessment, but has similar PSM rates to open procedures.

MANAGEMENT OF PSM

Many patients with PSMs will not progress, so there is controversy about whether they should be offered treatment, what the treatment should be and when it should be given. An important consideration with PSMs is the extent of residual disease; a persistently raised PSA level may be due to local recurrence or metastatic disease, and it is usually impossible to distinguish the cause with current staging techniques. Bone scintigraphy, CT and MRI are insufficiently sensitive at low PSA levels, whilst the utility of radio-immunoscinigraphy with ¹¹¹indium-capromab pentetide (ProstaScint) remains controversial. The time to PSA recurrence and PSA velocity have been used to help identify metastatic disease, but relying solely on this may deny treatment to patients with potentially curable disease, particularly as evidence is accumulating that salvage radiotherapy is most effective at low PSA levels.

ACTIVE SURVEILLANCE

Some studies have shown that RP with subsequent surveillance has an acceptable disease-free progression and long-term survival. One study of RP monotherapy showed overall and cancer-specific survival in pT3a tumours of 97.6% and 100%, respectively, after 68 months, while the 10-year probability of biochemical progression-free survival was calculated at 81.9% for patients with negative or single-focus PSMs [29]. Other studies reported 5- and 10-year progression-free survival rates for patients with PSMs of 78% and 55%, respectively. Connolly *et al.* [30] found no clear evidence linking a PSM to local recurrence.

The significance of extended lymph-node dissection for disease recurrence was recently highlighted. An extended lymph-node dissection involves the preservation of external iliac artery lymphatics but the removal of lymphatic tissue from the bifurcation of the common iliac artery proximally, along the internal iliac artery and vein, the angle between the external and internal iliac arteries and the obturator nerve, the obturator fossa and the external iliac vein up to the deep circumflex iliac vein. Studies show that this technique yields twice as many lymph nodes, with a two- to three-fold

increase in the percentage of positive nodes removed. More importantly, Di Blasio *et al.* [31] showed that removing ≈ 13 nodes sustained the lowest risk of progression, while there was a 16% and 8% risk of disease progression with 0–4 nodes and >14 nodes removed, respectively. As the margin status is irrelevant to outcomes if cancer involves lymph nodes, extended lymph-node dissection may delay biochemical progression and distant metastases in patients with PSMs. This in turn may reduce the need for adjuvant therapy after a PSM.

ADJUVANT THERAPY

After RP for clinically localized prostate cancer $\approx 35\%$ of patients will have additional treatment within 5 years. Many patients with adverse features such as a PSM will have residual disease, and are destined to relapse despite surgery. Adjuvant therapy for these patients may increase cure rates by delivering treatment soon after surgery, when the tumour burden is low and with an early phase of rapid growth that is more susceptible to treatment. Patients may also have better performance status than when their disease recurs.

Adjuvant radiotherapy has been extensively investigated in patients with high-risk features, including PSMs. Initial studies showed no clear survival benefits in patients with PSMs, nodal or seminal vesicle invasion. The 10-year survival rates for high-risk patients after surgery alone are 52–80%, compared to 60–76% in patients after surgery and adjuvant radiotherapy. In a recent study, when early salvage radiotherapy was initiated for biochemical recurrence after RP, the 4-year progression-free probability was 81% in patients with Gleason scores of 8–10 and PSMs when the PSA doubling time was >10 months, but decreased to 37% when the doubling time was <10 months [32]. That study found that, although patients had PSMs, early salvage radiotherapy would improve their progression-free survival if they had no seminal vesicle involvement, low Gleason scores, a PSA level of <2 ng/mL before radiotherapy and a PSA doubling time of >10 months. In another study, Eggener *et al.* [33] found that patients with PSMs after RP had no significant differences in their 4-year PSA-free, 4-year cancer-specific and 4-year overall survival, regardless of whether they had immediate adjuvant radiotherapy. After reviewing early studies of adjuvant and

delayed (salvage) radiotherapy, the American Society for Therapeutic Radiology and Oncology consensus panel concluded that a PSA level of up to 0.5 ng/mL after RP would not reduce the likelihood of cure with radiotherapy, but an increase to >1.5 ng/mL would significantly worsen the outcome. As PSMs do not necessarily predict the response to radiotherapy, and the PSA response to immediate and delayed radiotherapy is similar (PSA < 0.3 ng/mL), it remains unclear as to which approach to follow.

The recent European Organisation for Research and Treatment of Cancer (EORTC) 22911 study recruited patients with high-risk factors (including PSMs, capsule invasion and seminal vesicle invasion) and randomized them to immediate postoperative radiotherapy (median dose 60 Gy over 6 weeks) or a watchful-waiting policy. Both the local control rate and biochemical failure rate improved after immediate treatment. The biochemical progression-free survival rate at 5 years was 72.2% in the adjuvant arm, compared to 51.8% in the watchful-waiting group; the clinical progression-free survival at 5 years was 83.3% and 74.8%, respectively. Loco-regional failure was also significantly lower in the immediate adjuvant arm. All of these results were statistically significant [34].

There have been few studies outlining the benefits of adjuvant hormone therapy after RP. The first of these showed immediate adjuvant treatment with goserelin or orchidectomy reduced disease progression in patients with T1–2 and nodal metastases, from 77% to 18%, and increased their survival from 65% to 85% at a median follow-up of 7.1 years [35]. More recently, the Early Prostate Cancer trial showed that patients on 150 mg bicalutamide as an immediate adjuvant treatment, compared to placebo, after radical treatment had significantly better 5-year progression-free survival, particularly in the group with locally advanced disease [36,37]. However, the studies suggested lower survival in patients with organ-confined disease who were given adjuvant treatment. Early adjuvant hormone therapy may also reduce the risk of complications such as skeletal pain and spinal cord compression. It is unclear what the optimum period of androgen ablation is in these patients; this is important, as long-term therapy risks impotence, cognitive changes, anaemia, muscle weakness and osteoporosis, as well as impinging on the patients' quality

of life. At present, there are no randomized studies that show any advantage of adjuvant hormone therapy in patients with PSMs after RP. However, there are ongoing trials assessing the response of high-risk patients to a combination of adjuvant hormone treatment and chemotherapy (South West Oncology Group, SWOG, S9921, assessing mitoxantrone and prednisolone, and the Radiation Therapy Oncology Group, RTOG, P-9902 assessing paclitaxel, estramustine and etoposide).

The use of combined adjuvant therapy with hormone ablation and radiation has not been well studied. Miyake *et al.* [38] treated 38 patients with T3N0 or T3N1 prostate cancer with immediate adjuvant hormone ablation and radiotherapy, and compared their outcomes with 54 patients who received no treatment after their RP until they developed biochemical recurrence. In this non-randomized study, the 10-year biochemical recurrence-free, cancer-specific and overall survival rates were 86.7%, 90.9% and 78.7%, respectively. Although immediate treatment prolonged the disease-free interval, there was no difference in the cancer-specific and overall survival rates between the groups. At present there is no good evidence about the optimum time to commence hormone therapy or radiotherapy, and the duration of hormone treatment required. However, recently, a non-randomized study compared adjuvant radiotherapy alone with a short course of total androgen suppression 2 months before and 2 months concurrent with adjuvant radiotherapy in patients after RP [39]. Results showed that the 5-year overall and PSA relapse-free survival rates for the total androgen suppression and radiotherapy group was 57% and 100%, respectively, vs 31% and 87% in the group treated solely with radiotherapy. Four large studies (EORTC 22911, German cancer society ARO 96–02, RTOG-P-0011, SWOG 8794) are either underway or recently completed that will attempt to address the uncertainties relating to adjuvant radiotherapy with or without hormone ablation.

CONCLUSION

Although RP is used in patients with the assumption that there is no locally advanced or metastatic spread, PSM rates are still significant. As seen in previous studies, it is extremely difficult to predict a PSM outcome. However, refined surgical technique

regardless of the approach for RP or the clinical stage of the cancer may improve PSM rates. Patients with PSMs are at greater risk of progression, and the ability to stratify this risk is improving, together with other factors that may affect disease progression and survival.

Adjuvant treatment is often given to reduce the risk of recurrence and improve survival, despite a proportion of patients with PSMs not progressing. Uncertainties remain as to the most appropriate adjuvant therapy and when it should be given, particularly as it is usually unclear whether the patient has local residual disease or distant micrometastases. Results of ongoing studies and future research using neoadjuvant and adjuvant therapies are required to provide a better understanding of how to manage these patients.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Smith DS, Catalona WJ, Herschman JD. Longitudinal screening for prostate cancer with prostate-specific antigen. *JAMA* 1996; **276**: 1309–15
- Catalona WJ, Smith DS. 5-year tumor recurrence rates after anatomical radical retropubic prostatectomy for prostate cancer. *J Urol* 1994; **152**: 1837–42
- Cheng L, Darson ME, Bergstralh EJ, Slezak J, Myers RP, Bostwick DG. Correlation of margin status and extraprostatic extension with progression of prostate carcinoma. *Cancer* 1999; **86**: 1775–82
- Palisaar RJ, Noldus J, Graefen M, Erbersdobler A, Haese A, Huland H. Influence of nerve-sparing (NS) procedure during radical prostatectomy (RP) on margin status and biochemical failure. *Eur Urol* 2005; **47**: 176–84
- Boccon-Gibod L, Ravery V, Vordos D, Toublanc M, Delmas V, Boccon-Gibod L. Radical prostatectomy for prostate cancer: the perineal approach increases the risk of surgically induced positive margins and capsular incisions. *J Urol* 1998; **160**: 1383–5
- Epstein JI, Sauvageot J. Do close but negative margins in radical prostatectomy specimens increase the risk of postoperative progression? *J Urol* 1997; **157**: 241–3
- Freeland SJ, Aronson WJ, Presti JC Jr *et al.* The Search Database Study Group. Should a positive surgical margin following radical prostatectomy be pathological stage T2 or T3? Results from the Search Database. *J Urol* 2003; **169**: 2142–6
- Wieder JA, Soloway MS. Incidence, etiology, location, prevention and treatment of positive surgical margins after radical prostatectomy for prostate cancer. *J Urol* 1998; **160**: 299–315
- Hull GW, Rabbani F, Abbas F, Wheeler TM, Kattan MW, Scardino PT. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. *J Urol* 2002; **167**: 528–34
- Ward JF, Zincke H, Bergstralh EJ, Slezak JM, Myers RP, Blute ML. The impact of surgical approach (nerve bundle preservation versus wide local excision) on surgical margins and biochemical recurrence following radical prostatectomy. *J Urol* 2004; **172**: 1328–32
- Korman HJ, Leu PB, Huang RR, Goldstein NS. A centralized comparison of radical perineal and retropubic prostatectomy specimens: is there a difference according to the surgical approach? *J Urol* 2002; **168**: 991–4
- Erdogru T, Teber D, Frede T *et al.* Comparison of transperitoneal and extraperitoneal laproscopic radical prostatectomy using match-pair analysis. *Eur Urol* 2004; **46**: 312–20
- Brown JA, Garlitz C, Gomella LG *et al.* Pathologic comparison of laproscopic versus open radical retropubic prostatectomy specimens. *Urology* 2003; **62**: 481–6
- Salomon L, Levrel O, Anastasiadis AG *et al.* Outcome and complications of radical prostatectomy in patients with PSA <10ng/ml: comparison between the retropubic, perineal and laparoscopic approach. *Prostate Cancer Prostatic Dis* 2002; **5**: 285–90
- Epstein JI. Incidence and significance of positive margins in radical prostatectomy specimens. *Urol Clin North Am* 1996; **23**: 651–63
- Hall GS, Kramer CE, Epstein JI. Evaluation of radical prostatectomy specimens. A comparative analysis of sampling methods. *Am J Surg Pathol* 1992; **16**: 315–24
- D'Amico AV, Whittington R, Malkowicz SB *et al.* A multivariate analysis of clinical and pathological factors that predict for prostate specific antigen failure after radical prostatectomy for prostate cancer. *J Urol* 1995; **154**: 131–8
- Sofer M, Hamilton-Nelson KL, Civantos F, Soloway MS. Positive surgical margins after radical retropubic prostatectomy: the influence of site and number on progression. *J Urol* 2002; **167**: 2453–6
- Obek C, Sadek S, Lai S, Civantos F, Rubinowicz D, Soloway MS. Positive surgical margins with radical retropubic prostatectomy: anatomic site-specific pathologic analysis and impact on prognosis. *Urology* 1999; **54**: 682–8
- Salomon L, Anastasiadis AG, Levrel O *et al.* Location of positive surgical margins after retropubic, perineal and laproscopic radical prostatectomy for organ-confined prostate cancer. *Urology* 2003; **61**: 386–90
- Epstein JI, Pizov G, Walsh PC. Correlation of pathologic findings with progression after radical retropubic prostatectomy. *Cancer* 1993; **71**: 3582–93
- Grossfeld GD, Chang JJ, Broering JM *et al.* Impact of positive surgical margins on prostate cancer recurrence and the use of secondary cancer treatment: data from the CaPSURE database. *J Urol* 2000; **163**: 1171–7
- Blute ML, Bostwick DG, Bergstralh EJ *et al.* Anatomic site-specific positive margins in organ-confined prostate cancer and its impact on outcome after radical prostatectomy. *Urology* 1997; **50**: 733–9
- Shuford MD, Cookson MS, Chang SS *et al.* Adverse prognostic significance of capsular incision with radical retropubic prostatectomy. *J Urol* 2004; **172**: 119–23
- Ohori M, Abbas F, Wheeler TM, Kattan MW, Scardino PT, Lerner SP. Pathologic features and prognostic significance of prostate cancer in apical section determined by whole mount histology. *J Urol* 1999; **161**: 500–4
- Walsh PC, Marschke P, Ricker D, Burnett AL. Use of intraoperative video documentation to improve sexual function after radical retropubic prostatectomy. *Urology* 2000; **55**: 62–7
- Touijer K, Kuroiwa K, Saranchuk JW *et al.* Quality improvement in laproscopic radical prostatectomy for pT2 prostate cancer: impact of video documentation review on positive surgical margin. *J Urol* 2005; **173**: 765–8

- 28 Ahlering TE, Eichel L, Edwards RA, Lee DI, Skarecky DW. Robotic radical prostatectomy: a technique to reduce pT2 positive margins. *Urology* 2004; **64**: 1224–8
- 29 Isorna Martinez de la Riva S, Belon Lopez-Tomasety J, Marrero Dominguez R, Alvarez Cruz E, Santamaria Blanco P. [Radical prostatectomy as monotherapy for locally advanced prostate cancer (T3a): 12 years follow-up]. *Arch Esp Urol* 2004; **57**: 679–92
- 30 Connolly JA, Shinohara K, Presti JC Jr, Carroll PR. Local recurrence after radical prostatectomy: characteristics in size, location, and relationship to prostate-specific antigen and surgical margins. *Urology* 1996; **47**: 225–31
- 31 Di Blasio CJ, Fearn P, Seo HS *et al.* Association between number of lymph nodes removed and freedom from disease progression in patients receiving pelvic lymph node dissection during radical prostatectomy. *J Urol* 2003; **169**: 456
- 32 Stephenson AJ, Shariat SF, Zelefsky MJ *et al.* Salvage radiotherapy for recurrent prostate cancer after radical prostatectomy. *JAMA* 2004; **291**: 1325–32
- 33 Eggener SE, Roehl KA, Smith ND, Antenor JA, Han M, Catalona WJ. Contemporary survival results and the role of radiation therapy in patients with node negative seminal vesicle invasion following radical prostatectomy. *J Urol* 2005; **173**: 1150–5
- 34 Bolla M, Van Poppel P, Van Cangh K *et al.* Does post-operative radiotherapy (P-RXT) after radical prostatectomy (Px) improve progression-free survival (PFS) in pT3N0 prostate cancer (PC)? (EORTC 22911). *J Clin Oncol* 2004; **22**: 4504
- 35 Messing EM, Manola J, Sarosdy M, Wilding G, Crawford ED, Trump D. Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer. *N Eng J Med* 1999; **341**: 1781–8
- 36 Iversen P, Johansson JE, Lodding P *et al.* Bicalutamide (150mg) versus placebo as immediate therapy alone or as adjuvant to therapy with curative intent for early nonmetastatic prostate cancer: 5.3-year median follow-up from the Scandinavian Prostate Cancer Group Study Number 6. *J Urol* 2004; **172**: 1871–6
- 37 Wirth MP, See WA, McLeod DG, Iversen P, Morris T, Carroll K; Casodex Early Prostate Cancer Trialists' Group. Bicalutamide 150mg in addition to standard care in patients with localised or locally advanced prostate cancer: results from the second analysis of the early prostate cancer program at median follow-up of 5.4 years. *J Urol* 2004; **172**: 1865–70
- 38 Miyake H, Sakai I, Harada K, Hara I, Eto H. Long-term results of adjuvant hormonal therapy plus radiotherapy following radical prostatectomy for patients with pT3N0 or pT3N1 prostate cancer. *Int J Urol* 2004; **11**: 397–401
- 39 King CR, Presti JC Jr, Gill H, Brooks J, Hancock SL. Radiotherapy after radical prostatectomy: does transient androgen suppression improve outcomes? *Int J Radiat Oncol Biol Phys* 2004; **59**: 341–7

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Abbreviations: RP, radical prostatectomy; PSM(s), positive surgical margin(s); EORTC, European Organisation for Research and Treatment of Cancer; SWOG, South West Oncology Group; RTOG, Radiation Therapy Oncology Group.