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Platinum Priority – Editorial

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Will Favourable Functional Results with Salvage Robot-assisted Laparoscopic Radical Prostatectomy Increase the Uptake of Primary Focal Therapy for Localised Prostate Cancer?

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Focal therapy as a primary treatment for localised prostate cancer has the primary aims of eradication of the primary tumour and minimising post-treatment genitourinary dysfunction. It is seen by many as a conduit between active surveillance of low-risk prostate cancer and radical whole-gland treatment for significant-volume intermediate- or high-risk prostate malignancy. The natural history of prostate cancer progression has been linked to the dominant index lesion in the majority of men [1,2]. Although prostate cancer is usually a multifocal disease, ablation of the highest-grade clone or focus of tumour within the prostate using focal therapy allows for active surveillance of the remainder of the prostate, which may harbour low-risk, potentially non-life-threatening prostate malignancy. Concerns with regard to focal therapy include recurrence or persistence of in-field significant tumour in the ablation zone, development of clinically significant out-of-field prostate cancer, and the morbidity and functional and oncological outcomes of salvage whole-gland treatment.

In this issue of *European Urology*, Marconi et al. [3] review the oncological and functional outcomes and predictors of prostate cancer recurrence following salvage robot-assisted radical prostatectomy (s-RALP) for focal therapy failure. This important manuscript by experienced academic surgeon researchers provides a valuable insight into the outcomes of s-RALP for local recurrence after focal therapy.

This multicentre cohort of 82 patients undergoing s-RALP after focal therapy failure predominantly had intermediate-risk prostate cancer (76% of the cohort). High-intensity focused ultrasound was the most common form of focal therapy (69%). Focal ablation was performed in 60% and hemi-ablation in 30% of men. The median blood loss of 400 cm^3 and length of stay of 1 day is similar to the results in the robotic arm of the randomised open versus robotic radical prostatectomy trial [4]. The functional incontinence outcomes at 1 yr are also similar to the robotic arm of the prospective, controlled, nonrandomised LAPPRO study [5]. At 12 mo, using a definition of no pad usage, the patient-reported continence rate was 83%. Erections hard enough for penetration with or without the use of a phosphodiesterase inhibitor were achieved by 67% of the cohort at baseline and 14% at 12 mo. There were no intraoperative complications. All of the postoperative complications (6%) were Clavien-Dindo grade 1, apart from a vesicourethral anastomotic leak (grade 3b). The positive margin rate of 13% is consistent with international standards for primary RALP, including the open versus RALP randomised controlled trial [4].

Of some concern is the biochemical recurrence-free survival of only 21% with in-field recurrence after focal therapy, compared to 55% for out-of-field recurrence (hazard ratio 3.96; $p = 0.02$). In a cohort with predominantly intermediate risk, this raises concern regarding the oncological outcomes compared with primary radical prostatectomy for intermediate-risk prostate cancer. The authors appropriately conclude that men undergoing s-RALP for recurrent disease after focal therapy should be counselled regarding the potential requirement for multimodal treatment, with men experiencing in-field recurrence at the focal therapy ablation site having almost four

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times the risk of developing biochemical failure after s-RALP. Like all retrospective studies, selection and treatment bias cannot be excluded. Men who develop in-field recurrence after focal therapy have potentially biologically aggressive tumours and may also be at higher risk of biochemical relapse following RALP as primary treatment for their prostate cancer.

The prostate-specific antigen era has led to the identification of lower-volume prostate cancer at diagnosis. Although controversy exists regarding the role of negative multiparametric magnetic resonance imaging (mpMRI) in ruling out the need for prostate biopsy [6], mpMRI before prostate biopsy does increase the detection of clinically significant prostate cancer [7]. The addition of mpMRI followed by targeted biopsies of an index lesion with a Prostate Imaging-Reporting and Data system score of 3–5 combined with an extended systematic mapping biopsy will increase the detection of a target cancer suitable for focal therapy.

The scientific evidence regarding the role of focal therapy for primary treatment of newly diagnosed prostate cancer is far from robust. No consensus has been reached on the ideal candidates for focal therapy or the definition of what constitutes focal therapy failure. There are multiple forms of focal therapy, including high-intensity focused ultrasound, cryotherapy, brachytherapy (low dose and high dose rates), laser interstitial thermotherapy, radiofrequency ablation, and irreversible electroporation. The focal therapy techniques also vary from focal to extended hemi-ablation. Only three studies have published data beyond 5 yr. It will take large-scale randomised controlled trials and more than a decade of follow-up to establish oncological noninferiority over radical whole-gland therapies and superiority over active surveillance [8]. However, this concise, well-written manuscript by Marconi et al. [3] provides urological surgeons with confidence that salvage of focal therapy failures has perioperative complications and functional outcomes similar to those for RALP in the primary setting. However, oncological outcomes for in-field recurrence are suboptimal. This study emphasises the importance of in-field clearance after focal therapy. MRI alone appears to be inadequate [9] and early biopsy after focal therapy may need to be a routine requirement for focal therapy programs, possibly with incorporation of prostate-specific membrane antigen-based positron emission tomography and genomics. Much more scientific research is required to evaluate the cohort of men at risk of in-field recurrence before the widespread adoption of focal therapy outside of clinical trials or prospective evaluation in tertiary referral centres.

Conflicts of interest: The author has nothing to disclose.

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