



Focal Therapy for Localised Prostate Cancer: Patient Selection and Follow-Up Protocols

Ruby Ramanathan^{1*}, Tariq Lim², Mai Ngo³

¹Department of Medical Sciences, Irrawaddy School of Medical Sciences, Jordan

²Department of Medical Sciences, Limpopo Center for Medical Sciences, Sweden

³Department of Medical Sciences, Pampas Institute for Advanced Medical Sciences, Kenya

Article Info

Volume 1, Issue 1, 2026

doi: [10.62715/ijua.2026.v1.i1.pp8-14](https://doi.org/10.62715/ijua.2026.v1.i1.pp8-14)

Received: 03 April 2026

Accepted: 27 May 2026

Published: 27 July 2026

Abstract

Focal therapy aims to destroy the clinically significant part of a prostate cancer while leaving the remainder of the gland, the sphincter and the neurovascular bundles untouched. It occupies the ground between active surveillance, which accepts the risk of progression, and radical surgery or radiotherapy, which accept a risk of incontinence, erectile dysfunction and bowel symptoms. Whether it succeeds depends less on the energy source than on two decisions made around the procedure: which men are offered it, and how they are watched afterwards. This narrative review considers both. It sets out the rationale that rests on the index lesion, the role of multiparametric magnetic resonance imaging and combined targeted and systematic biopsy in localising disease, and the selection criteria on which international consensus panels have converged. It then examines follow-up, where prostate-specific antigen has no validated definition of failure, imaging of the treated gland requires its own reading rules, and a control biopsy remains the reference test. Published series report good preservation of urinary and sexual function and acceptable medium-term cancer control, but randomised comparisons with standard care are lacking, and guidelines continue to recommend treatment within trials or prospective registries.

Keywords: Focal therapy, Prostate cancer, Patient selection, Multiparametric MRI, High-intensity focused ultrasound, Follow-up

© 2026 Ruby Ramanathan et al. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

1. Introduction

Men with localised prostate cancer have long been offered a choice between treating the whole gland and treating nothing. The ProtecT trial showed that, at ten years, deaths from prostate cancer were few whether men were assigned to active monitoring, radical prostatectomy or radiotherapy, although progression and metastasis were more frequent with monitoring (Hamdy et al., 2016). The companion report on patient-reported outcomes documented the price of radical treatment: urinary leakage and loss of erectile function were worst after surgery, and bowel symptoms after radiotherapy (Donovan et al., 2016). Many men, particularly those with intermediate-risk disease, find neither option comfortable.

* Corresponding author: Ruby Ramanathan, Department of Medical Sciences, Irrawaddy School of Medical Sciences, Jordan. E-mail: ruby.ramanathan@irrawaddy.edu

© 2026 Ruby Ramanathan et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Focal therapy was proposed as a third course. Onik *et al.* (2002) described cryoablation confined to the side of the gland containing tumour, with the explicit aim of preserving potency, and likened the idea to lumpectomy for breast cancer. Since then high-intensity focused ultrasound, cryotherapy, irreversible electroporation, vascular-targeted photodynamic therapy, focal laser ablation and focal brachytherapy have all been used to ablate part of the prostate (Valerio *et al.*, 2017). The technologies differ, but the clinical questions they raise are the same.

This review addresses two of those questions: how patients should be selected and how they should be followed. Both have been the subject of formal consensus exercises, and both remain less settled than the volume of publication might suggest.

2. Approach of This Review

The article is a narrative review of the published literature. It relies on the diagnostic trials that underpin modern lesion localisation, on prospective and registry series of focal therapy, on systematic reviews of those series, and on Delphi consensus statements and guidelines. No formal search strategy was applied, and the sources were chosen for their influence on current practice. Salvage focal therapy after radiotherapy is not covered.

3. Rationale: The Index Lesion

Prostate cancer is usually multifocal. Whole-mount studies of prostatectomy specimens found several separate tumours in most glands, but the largest focus accounted for most of the tumour volume and the secondary foci were typically small and of low grade (Wise *et al.*, 2002). Genomic analysis of men who died of metastatic disease indicated that their metastases shared a single clonal origin (Liu *et al.*, 2009). From these observations came the index lesion hypothesis: that one dominant focus drives the natural history of the disease, and that destroying it may be sufficient while small low-grade foci elsewhere are observed (Ahmed, 2009).

The hypothesis is reasonable and not proven. The lethal clone is not always the largest lesion, and the behaviour of untreated tissue over decades is unknown. Focal therapy is therefore best understood as treatment combined with continued surveillance of the remaining gland, a point that shapes both selection and follow-up.

4. Patient Selection

Selection has three components: the grade and extent of the cancer, the confidence with which it has been localised, and the characteristics of the man himself. Table 1 summarises the criteria on which consensus statements broadly agree and the points that remain open.

4.1. Risk group and grade

Early series enrolled many men with low-risk cancer, who would now be advised to choose active surveillance. Expert panels have since shifted the indication towards intermediate-risk disease. The consensus meeting reported by Donaldson *et al.* (2015) concluded that focal therapy should be directed mainly at men with intermediate-risk cancer and that low-grade, low-volume disease outside the treatment field could be left untreated. The international Delphi project led by Tay *et al.* (2017) reached a similar position. In the grade group system adopted by the International Society of Urological Pathology (Epstein *et al.*, 2016), the typical candidate has a localised grade group 2 lesion; opinion is divided on grade group 3, and high-risk disease is generally regarded as unsuitable outside research.

4.2. Localising the cancer

Focal treatment is only as good as the map on which it is based. The PROMIS study showed that multiparametric magnetic resonance imaging (mpMRI) was considerably more sensitive than transrectal ultrasound-guided systematic biopsy for clinically significant cancer, using transperineal template mapping as the reference (Ahmed *et al.*, 2017). The PRECISION trial then showed that an MRI-targeted

biopsy pathway detected more significant cancers and fewer insignificant ones than standard systematic biopsy ([Kasivisvanathan *et al.*, 2018](#)). Reporting is standardised by the Prostate Imaging Reporting and Data System ([Turkbey *et al.*, 2019](#)).

Table 1: Selection considerations for primary focal therapy, as reflected in consensus statements and guidelines

Domain	Generally accepted	Still debated	Sources
Risk group	Intermediate-risk disease, chiefly grade group 2	Grade group 3; small high-grade lesions	Donaldson <i>et al.</i>, 2015 ; Tay <i>et al.</i>, 2017
Low-risk disease	Active surveillance is the preferred strategy	Treatment of large-volume grade group 1	Mottet <i>et al.</i>, 2021
Imaging	Multiparametric MRI before biopsy and before treatment	Role of PSMA PET and ultrasound variants	Ahmed <i>et al.</i>, 2017 ; Turkbey <i>et al.</i>, 2019
Biopsy	Targeted cores plus systematic sampling of the untreated gland	Need for transperineal template mapping	Kasivisvanathan <i>et al.</i>, 2018 ; Tay <i>et al.</i>, 2017
Untreated foci	Small low-grade foci outside the field may be observed	Size limit of acceptable untreated disease	Donaldson <i>et al.</i>, 2015
Patient factors	Sufficient life expectancy; willingness to attend follow-up	Gland size, calcification, prior surgery	Valerio <i>et al.</i>, 2017

Imaging does not see everything. Small and low-grade foci are often invisible, and some significant tumours are missed. For that reason consensus panels ask for systematic sampling of the areas that will not be treated in addition to targeted cores from the visible lesion ([Tay *et al.*, 2017](#)). Transperineal template mapping gives the most complete picture but at the cost of anaesthesia and morbidity, and with good-quality mpMRI most panels no longer consider it mandatory.

4.3. Matching the patient and the energy

The systematic review by [Valerio *et al.* \(2017\)](#) found that high-intensity focused ultrasound and cryotherapy had the largest evidence base, with other sources at an earlier stage of evaluation. Choice of energy is influenced by lesion position. Transrectal ultrasound energy reaches posterior tumours readily, whereas anterior lesions in large glands may be better suited to cryotherapy or to needle-based techniques. Men should also understand before treatment that focal therapy commits them to a schedule of tests, and that a proportion will need a second focal procedure or a later radical treatment. A man who is unlikely to attend surveillance is not a good candidate.

5. What Published Series Show

The prospective development study of focal high-intensity focused ultrasound by [Ahmed *et al.* \(2012\)](#) established that unifocal and multifocal lesions could be ablated with a low rate of genitourinary side effects. Focal cryotherapy has been reported from a large national registry ([Ward and Jones, 2012](#)). A multicentre series from the United Kingdom reported five-year outcomes in men of whom most had intermediate- or high-risk cancer ([Guillaumier *et al.*, 2018](#)), later extended to a larger cohort with longer follow-up ([Reddy *et al.*, 2022](#)). A phase 2b study of MRI-guided focused ultrasound enrolled men with intermediate-risk disease ([Ehdaie *et al.*, 2022](#)). Across these reports continence was preserved in the great majority and erectile function in most, while a minority of men required retreatment or went on to radical therapy.

The limits of this evidence are plain. Almost all of it is single-arm. The one large randomised trial, of padeliporfin vascular-targeted photodynamic therapy, compared treatment with active surveillance in men with low-risk cancer, a group for whom intervention is now seldom recommended ([Azzouzi *et al.*, 2017](#)). An updated systematic review found that the quality of the evidence had improved little over five years and that definitions of success still varied between studies ([Hopstaken *et al.*, 2022](#)). European

guidelines accordingly advise that focal therapy be offered within a clinical trial or a well-designed prospective registry (Mottet et al., 2021).

6. Follow-Up Protocols

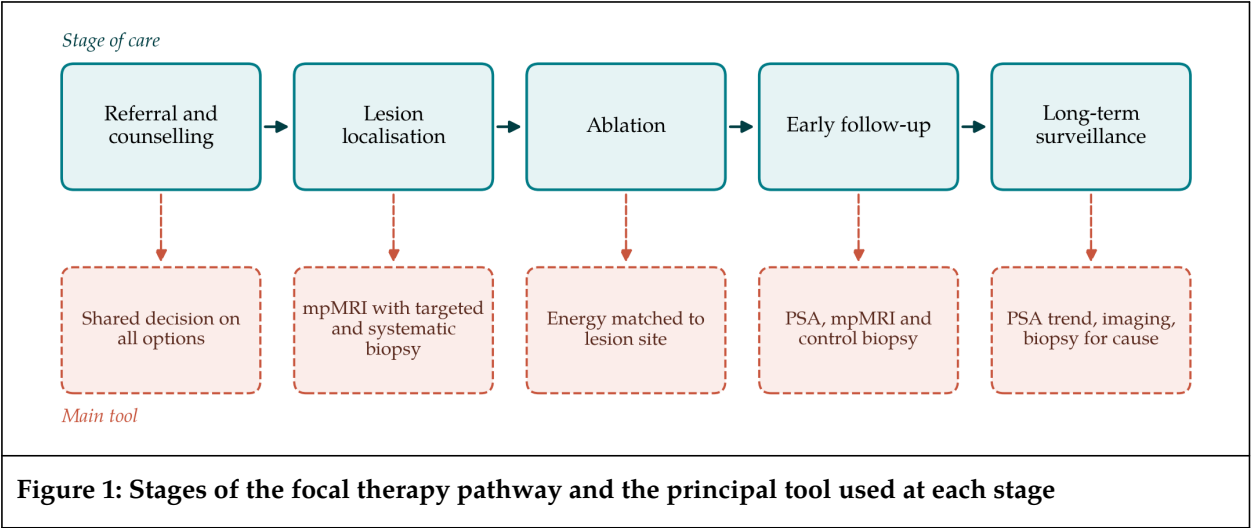
Follow-up after focal therapy has to answer two questions at once: whether the ablation destroyed the target, and whether significant cancer has appeared in the untreated gland. Figure 1 places follow-up in the pathway of care, with the main tool used at each stage.

6.1. Prostate-specific antigen

Prostate-specific antigen (PSA) falls after ablation but does not become undetectable, because viable prostate tissue remains. No threshold has been validated to define failure. The Phoenix definition of nadir plus 2 ng/mL was derived for radiotherapy (Roach et al., 2006) and has been borrowed by some focal therapy series without evidence that it predicts clinical outcomes in this setting. Consensus statements therefore treat PSA as a trend to be watched and a trigger for further tests, not as an endpoint in itself (Muller et al., 2015; Lebastchi et al., 2020).

6.2. Imaging the treated gland

Multiparametric MRI is the imaging standard after treatment as before it, but the ablated zone looks different from untreated prostate. Scarring, loss of volume and altered enhancement make the pre-treatment scoring rules unreliable. Early contrast-enhanced imaging can confirm that the intended zone has been devascularised; later scans look for focal early enhancement and restricted diffusion at the margin of the cavity. A dedicated scoring proposal for the treated prostate, Prostate Imaging after Focal Ablation, has been published to make reporting more consistent (Giganti et al., 2023). Its performance against biopsy has still to be established in independent cohorts.



6.3. Control biopsy

Histology remains the reference. The Delphi project on follow-up recommended that men be followed for at least five years, with PSA at regular intervals, mpMRI and a biopsy of the treated area within about the first year (Muller et al., 2015). The later multidisciplinary consensus endorsed a protocol biopsy combining targeted cores from the ablation zone with systematic sampling of the rest of the gland, and proposed standard terms that separate in-field recurrence, which reflects failure of ablation, from out-of-field disease, which reflects selection or new tumour (Lebastchi et al., 2020). The distinction matters because the two call for different responses and say different things about a programme's quality.

6.4. Defining failure and reporting function

There is broad agreement that small amounts of grade group 1 cancer on control biopsy need not be

counted as failure, and that clinically significant cancer in the treated field should be. Beyond that, endpoints differ: some series report any positive biopsy, others freedom from radical or systemic treatment. Comparison between centres is unreliable until a common definition is used. Functional outcomes should be collected with validated patient-completed questionnaires at baseline and at fixed intervals, since preservation of continence and erectile function is the reason for choosing focal therapy in the first place.

How long and how intensively to continue surveillance is unresolved. After a negative control biopsy, most protocols rely on PSA at intervals of several months and periodic mpMRI, with further biopsy prompted by a rising PSA or a new imaging finding. The untreated gland remains at risk indefinitely, so follow-up in effect merges with active surveillance of the remaining prostate. Men in whom significant cancer is found may be offered repeat focal ablation, surgery or radiotherapy, and the feasibility and morbidity of these salvage treatments form part of what a programme should report.

7. Gaps and Future Work

The central gap is comparative evidence. Randomised trials against radical treatment have proved difficult to recruit, because men who seek focal therapy are often unwilling to be allocated to surgery. Prospective registries with agreed selection criteria, a fixed biopsy schedule and standard definitions are the practical alternative, and their value depends on completeness of follow-up. Long-term data are also needed: prostate cancer evolves over decades, and most series report medians of only a few years. Further questions concern the place of prostate-specific membrane antigen imaging in selection, the validation of post-ablation MRI scoring, and whether a safe schedule can be defined that spares men repeated biopsy when imaging and PSA are reassuring.

8. Conclusion

Focal therapy offers men with localised, well-characterised, intermediate-risk prostate cancer a means of treating the dominant lesion with a low risk of incontinence and a moderate risk to erectile function. Its results depend on accurate localisation with mpMRI and combined biopsy, on restricting treatment to men whose disease fits the index lesion model, and on disciplined surveillance in which a control biopsy, not PSA alone, determines success. The evidence is still largely uncontrolled. Until comparative and long-term data are available, treatment within prospective registries or trials, with candid counselling about retreatment, is the defensible standard.

Conflict of interest

To be declared by the author(s) before publication.

Funding

To be declared by the author(s) before publication.

References

- Ahmed, H.U. (2009). [The index lesion and the origin of prostate cancer](#). *New England Journal of Medicine*, 361(17): 1704-1706.
- Ahmed, H.U., El-Shater Bosaily, A., Brown, L.C., et al. (2017). [Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer \(PROMIS\): a paired validating confirmatory study](#). *Lancet*, 389(10071): 815-822. [https://doi.org/10.1016/S0140-6736\(16\)32401-1](https://doi.org/10.1016/S0140-6736(16)32401-1)
- Ahmed, H.U., Hindley, R.G., Dickinson, L., Freeman, A., Kirkham, A.P., Sahu, M., Scott, R., Allen, C., Van der Meulen, J. and Emberton, M. (2012). [Focal therapy for localised unifocal and multifocal prostate cancer: a prospective development study](#). *Lancet Oncology*, 13(6): 622-632. [https://doi.org/10.1016/S1470-2045\(12\)70121-3](https://doi.org/10.1016/S1470-2045(12)70121-3)
- Azzouzi, A.-R., Vincendeau, S., Barret, E., et al. (2017). [Podeliporfin vascular-targeted photodynamic](#)

- therapy versus active surveillance in men with low-risk prostate cancer (CLIN1001 PCM301): an open-label, phase 3, randomised controlled trial. *Lancet Oncology*, 18(2): 181-191. [https://doi.org/10.1016/S1470-2045\(16\)30661-1](https://doi.org/10.1016/S1470-2045(16)30661-1)
- Donaldson, I.A., Alonzi, R., Barratt, D., et al. (2015). Focal therapy: patients, interventions, and outcomes: a report from a consensus meeting. *European Urology*, 67(4): 771-777.
- Donovan, J.L., Hamdy, F.C., Lane, J.A., et al. (2016). Patient-reported outcomes after monitoring, surgery, or radiotherapy for prostate cancer. *New England Journal of Medicine*, 375(15): 1425-1437. <https://doi.org/10.1056/NEJMoa1606221>
- Ehdaie, B., Tempany, C.M., Holland, F., et al. (2022). MRI-guided focused ultrasound focal therapy for patients with intermediate-risk prostate cancer: a phase 2b, multicentre study. *Lancet Oncology*, 23(7): 910-918.
- Epstein, J.I., Egevad, L., Amin, M.B., Delahunt, B., Srigley, J.R. and Humphrey, P.A. (2016). The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. *American Journal of Surgical Pathology*, 40(2): 244-252. <https://doi.org/10.1097/PAS.0000000000000530>
- Giganti, F., Dickinson, L., Orczyk, C., Haider, A., Freeman, A., Emberton, M., Allen, C. and Moore, C.M. (2023). Prostate Imaging after Focal Ablation (PI-FAB): a proposal for a scoring system for multiparametric MRI of the prostate after focal therapy. *European Urology Oncology*.
- Guillaumier, S., Peters, M., Arya, M., et al. (2018). A multicentre study of 5-year outcomes following focal therapy in treating clinically significant nonmetastatic prostate cancer. *European Urology*, 74(4): 422-429. <https://doi.org/10.1016/j.eururo.2018.06.006>
- Hamdy, F.C., Donovan, J.L., Lane, J.A., et al. (2016). 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *New England Journal of Medicine*, 375(15): 1415-1424. <https://doi.org/10.1056/NEJMoa1606220>
- Hopstaken, J.S., Bomers, J.G.R., Sedelaar, M.J.P., Valerio, M., Fütterer, J.J. and Rovers, M.M. (2022). An updated systematic review on focal therapy in localized prostate cancer: what has changed over the past 5 years? *European Urology*, 81(1): 5-33.
- Kasivisvanathan, V., Rannikko, A.S., Borghi, M., et al. (2018). MRI-targeted or standard biopsy for prostate-cancer diagnosis. *New England Journal of Medicine*, 378(19): 1767-1777. <https://doi.org/10.1056/NEJMoa1801993>
- Lebastchi, A.H., George, A.K., Polascik, T.J., et al. (2020). Standardized nomenclature and surveillance methodologies after focal therapy and partial gland ablation for localized prostate cancer: an international multidisciplinary consensus. *European Urology*, 78(3): 371-378.
- Liu, W., Laitinen, S., Khan, S., et al. (2009). Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer. *Nature Medicine*, 15(5): 559-565. <https://doi.org/10.1038/nm.1944>
- Mottet, N., van den Bergh, R.C.N., Briers, E., et al. (2021). EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer, 2020 update. Part 1: screening, diagnosis, and local treatment with curative intent. *European Urology*, 79(2): 243-262. <https://doi.org/10.1016/j.eururo.2020.09.042>
- Muller, B.G., van den Bos, W., Brausi, M., et al. (2015). Follow-up modalities in focal therapy for prostate cancer: results from a Delphi consensus project. *World Journal of Urology*, 33(10): 1503-1509.
- Onik, G., Narayan, P., Vaughan, D., Dineen, M. and Brunelle, R. (2002). Focal "nerve-sparing" cryosurgery for treatment of primary prostate cancer: a new approach to preserving potency. *Urology*, 60(1): 109-114.
- Reddy, D., Peters, M., Shah, T.T., et al. (2022). Cancer control outcomes following focal therapy using high-intensity focused ultrasound in 1379 men with nonmetastatic prostate cancer: a multi-institute 15-year experience. *European Urology*, 81(4): 407-413.
- Roach, M., Hanks, G., Thames, H., Schellhammer, P., Shipley, W.U., Sokol, G.H. and Sandler, H. (2006). Defining biochemical failure following radiotherapy with or without hormonal therapy in men with

- clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. *International Journal of Radiation Oncology, Biology, Physics*, 65(4): 965-974. <https://doi.org/10.1016/j.ijrobp.2006.04.029>
- Tay, K.J., Scheltema, M.J., Ahmed, H.U., et al. (2017). Patient selection for prostate focal therapy in the era of active surveillance: an International Delphi Consensus Project. *Prostate Cancer and Prostatic Diseases*, 20(3): 294-299. <https://doi.org/10.1038/pcan.2017.8>
- Turkbey, B., Rosenkrantz, A.B., Haider, M.A., et al. (2019). Prostate Imaging Reporting and Data System Version 2.1: 2019 update of Prostate Imaging Reporting and Data System Version 2. *European Urology*, 76(3): 340-351. <https://doi.org/10.1016/j.eururo.2019.02.033>
- Valerio, M., Cerantola, Y., Eggener, S.E., Lepor, H., Polascik, T.J., Villers, A. and Emberton, M. (2017). New and established technology in focal ablation of the prostate: a systematic review. *European Urology*, 71(1): 17-34. <https://doi.org/10.1016/j.eururo.2016.08.044>
- Ward, J.F. and Jones, J.S. (2012). Focal cryotherapy for localized prostate cancer: a report from the national Cryo On-Line Database (COLD) Registry. *BJU International*, 109(11): 1648-1654.
- Wise, A.M., Stamey, T.A., McNeal, J.E. and Clayton, J.L. (2002). Morphologic and clinical significance of multifocal prostate cancers in radical prostatectomy specimens. *Urology*, 60(2): 264-269.