Oncology

Focal High-intensity Focussed Ultrasound Partial Gland Ablation for the Treatment of Localised Prostate Cancer: A Report of Medium-term Outcomes From a Single-center in the United Kingdom

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OBJECTIVE To report our intermediate outcomes of the use of focal ablation for treating significant unilateral prostate cancer. This technique was adopted in our center 10 years ago. With improving diagnostic accuracy of index prostate cancer lesions and a low side-effect profile, use of focal high intensity focused ultrasound (HIFU) ablation is increasing.

METHODS Patients were diagnosed using prostate specific antigen (PSA), multiparametric magnetic resonance imaging, and template transperineal biopsies. Focal ablation of significant cancer was performed with the Sonablate device. Follow-up consisted of magnetic resonance imaging scanning, PSA, validated questionnaires, biopsy for cause, and redo HIFU if required as part of the treatment strategy.

RESULTS A total of 107 men underwent focal HIFU. In total, 88% had intermediate/high risk disease, and the mean pre-HIFU PSA was 7.7. A total of 31% had high volume Gleason 6 disease, 55% had Gleason 3+4 disease, and 13% had Gleason ≥ 4+3 disease. In total, 54 men received a hemiablation, 10 a focal ablation, and 43 a quadrant ablation. Median follow-up was 30 months, subjects' PSA dropped to an average 71% nadir. A total of 8% had biochemical recurrence and 11% required adjuvant treatment. Freedom from additional procedures for clinically significant recurrent disease, including redo-HIFU, was 85.5%. Postoperative complications included 1% new use of pads, 1.9% urethral stricture, 2.8% post-HIFU TURP, and new onset ED of 14%.

CONCLUSION In a carefully chosen cohort of patients for focal HIFU our results suggest acceptable oncological control with minimal postoperative morbidity. Further studies are required to establish this technique as a less morbid alternative to radical therapy. UROLOGY 00: 1–7, 2019. © 2019 Elsevier Inc.

In recent years, the life expectancy for men has been rapidly increasing and more men are being diagnosed with prostate cancer than ever before.[1-3] While radical treatment options such as prostatectomy and radiation therapy produce excellent oncological outcomes, there is a risk of significant side-effects. This has led to the introduction of focal therapy for prostate cancer which can reduce the inevitable collateral damage to the adjacent structures to the prostate which occurs during surgery or radiotherapy.[4]

High intensity focused ultrasound (HIFU) can be a whole gland treatment or only targeting the affected portion of the prostate gland. Publications from different international centres report 10-year freedom from metastasis and prostate cancer specific survival (CSS) rates following whole gland ablation with HIFU for the primary treatment of localized prostate cancer.[5-8] These reports demonstrate 10 year CSS, 10 year metastasis free survival (MFS), and 5 year biochemical disease free survivial (BDFS) that is near equivalent to radical prostatectomy and radiation therapy but with a superior morbidity profile to these standard therapies, especially in terms of incontinence and erectile dysfunction.[5,7,9]

The underlying principle of partial gland ablation is that only the portion of the prostate with evidence of clinically significant prostate cancer is treated, while any

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remaining nonclinically significant cancer, and any uninvolved prostate tissue, is monitored over time.

While there have been numerous published studies that attest to the efficacy and superior side effect profile of focal ablation of prostate cancer using HIFU, there is continued concern that the experience with focal therapy using HIFU is fragmented and of short duration.[9,10] This paper examines the medium-term outcomes for consecutive patients undergoing focal HIFU treatment in a single centre in the United Kingdom.

MATERIALS AND METHODS

Diagnosis of prostate cancer in our patients was performed using magnetic resonance imaging (MRI) scanning and prostatic biopsy. Targeted disease was localized prior to treatment using multiparametric MRI with a 1•5 T magnetic field strength and pelvic phased-array coils. Sequences included T2-weighting, dynamic gadolinium contrast-enhancement, and diffusion-weighting. Template-prostate-mapping biopsies were done under general anesthesia with the prostate sampled at 5 mm intervals. Two biopsies were taken at the same grid coordinate if the prostate was longer than the standard length of a biopsy core. All patients were discussed in a multidisciplinary team meeting to ensure that focal treatment was appropriate and were subsequently offered the opportunity to be part of a research trial. Patients with anterior tumours within a large prostate gland (greater than 40 cm^3) were not selected for HIFU. Those with smaller glands and anterior tumours, or very apical lesions were carefully counseled regarding their risks but were offered treatment if it was felt that an appropriate treatment margin could be applied safely.

Men underwent focal ablation with a transrectal HIFU device (Sonablate 500; SonaCare Medical, Charlotte, NC) under general anaesthetic. Transmission of sound waves transrectally was achieved by placing the probe in a condom filled with chilled circulating degassed water, producing a pseudoellipsoid lesion approximately 10 mm × 3 mm, referred to as elemental lesion, with its long axis at right angles to the transducer. These elemental lesions are combined in 3 dimensions to cover the region designated for ablation. Tissue destruction is produced by thermal, mechanical, and cavitation effects to produce a clearly demarcated region of coagulative necrosis surrounded by normal tissue on microscopic examination.

The location of tissue to be ablated was determined by cognitively registering the tissue that was deemed suspicious on MRI, and confirmed on biopsy, with ultrasound images taken by the Sonablate probe after insertion into the rectum. Sonablate provides the flexibility to design a custom plan depending on the location and the extent of the tissue targeted for ablation. Using the registered location and the volume of suspect tissue as seen on the MRI, men received either a focal ablation (a freeform region within the gland), a hemiablation (1 entire half of the gland), or a quadrant ablation (1 complete quadrant of the gland). For this cohort of men, a treatment protocol was designed that uniformly retreated anterior zones within the targeted volume in all men. This was an attempt to ensure patients with anterior tumours weren't undertreated, which has been a long-held concern leading to patients being excluded from some studies if they had anterior tumours in even modest sized prostates.[11]

After ablation, a urethral catheter was placed on free drainage into a urinary leg-bag for 3-5 days postoperatively. All men were given ciprofloxacin and oral analgesia (paracetamol) for 5 days. A contrast-enhanced MRI was performed 7-10 days after focal HIFU for the first 30 patients to confirm the area of ablation, as shown by a confluent perfusion deficit, ensuring that the treatment was likely to have achieved appropriate gland coverage.

Follow-up consisted of clinic visits at 1 month, 3 months, 6 months, and 12 months for prostate specific antigen (PSA) measurement and adverse event reporting. PSA failure was defined using the Stuttgart criteria.[12] Patients underwent further MPMRI at 12 months post-treatment to decide on further investigation and follow-up protocols. A subset of men who participated in clinical trials filled in validated questionnaires at each clinic visit, as well as an additional clinic visit at 9 months with a PSA. Functional outcomes were investigated if patients reported troublesome symptoms of lower urinary tract symptoms or erectile dysfunction. Repeat prostatic biopsy was undertaken at 12 months and 36 months for those patients involved in a trial and based on clinical suspicion of recurrent/residual/contralateral disease for other patients. Decisions regarding retreatment or salvage treatment were guided by the PSA, initial and subsequent histology, and MRI scans. Patients requiring retreatment were carefully counseled regarding their remaining options, which most frequently consisted of repeat HIFU or salvage radical prostatectomy. Low, intermediate, and high-risk disease were classified using the D'Amico system.[13] All patients within this study were subject to either local approval from the Trust Clinical Governance Board or ethical approval as part of their research study. All data was collected prospectively at the time of the HIFU treatment or subsequent follow-up visits. Statistical calculations were computed using SPSS statistics version 22 and significance was taken when $P < .05$.

RESULTS

A total of 107 men have had focal HIFU in our study centre and been followed up for 12 months or greater. The median length of follow-up for this cohort of patients was 30 months (range 12 months-9 years). The mean age of patients was 66 years (range 47-81). Greater than half (54) of the patients underwent a hemiablation procedure with 10 receiving a targeted focal procedure and 43 a quadrant ablation. Two-thirds (66%) had intermediate risk prostate cancer whilst 12% had low risk and 22% high risk, according to NCCN criteria. The mean prostate volume was 41 cm^3 (range 15-105). The Gleason grading, clinical T stage, and preprocedure biopsy information feature in **Table 1**.

Table 1. Gleason grading and preprocedure biopsy information ($n = 107$)

Characteristics	*n*
Gleason score	
3 + 3	32
3 + 4	60
4 + 3	14
4 + 4	1
T stage	
T1	9
T2	90
T3a	8
Biopsies, mean (range)	
Total cores	50 (6-101)
Total positive cores	6 (1-25)
Maximum cancer core length (mm)	6 (1-18)

Table 2. PSA (μg/L) results ($n = 107$)

Timing	Value
Pre-HIFU, mean (range)	7.7 (1.2-26.2)
Nadir	2.2 (0.0-12.2)
3 months post	2.8 (0-18.4)
12 months post	3.4 (0.2-15.5)
24 months post	3.3 (0.2-8.3)

Table 3. Secondary treatments ($n = 107$)

Treatment	Value
Salvage radiotherapy, *n* (%)	4 (3.7%)
Salvage prostatectomy	6 (5.6%)
Repeat focal HIFU	12 (11.2%)
Contralateral focal treatment	2 (1.9%)
Androgen deprivation therapy	2 (1.9%)

PSA characteristics pre- and postprocedure can be seen in Table 2. The average time to PSA failure for relevant patients was 37 months. A total of 16 (11%) patients had PSA defined biochemical failure according to the Stuttgart criteria. Of these, 3 were in the low risk group, 7 in the intermediate risk group, and 6 were high risk. Regarding their mode of treatment, 9 of these 16 patients had focal HIFU hemiablation, 5 were treated with true focal ablation, and 2 were treated by quandrant ablation. Figure 1 shows the survival from PSA failure for patients in each risk group.

Regarding the 22 patients who underwent repeat postprocedure biopsy for cause (as opposed to a biopsy as part of a trial), 12 had residual Gleason 3+3 disease and 6 had Gleason 7 disease. Of these patients, 6 had focal ablation, 4 had hemiablation, and 2 had a quadrant ablation. Eleven of these patients were in the intermediate risk group. Fifty-one patients (32%) were eligible to participate in a HIFU trial. Thirty-two were part of the INDEX trial, 14 joined the PART trial, and 5 were included in the NCRN FOCAL trial. Forty-five of these patients had a posttreatment biopsy. The majority ($n = 34/45$) were systematic and the rest (11/45) were systematic combined with a cognitively targeted biopsy according to the study protocol they were participating in. The biopsy strategy varied between studies and was performed between 6 months and 3 years from initial treatment and sometimes on multiple occasions. A total of 33 patients (73%) had a negative biopsy after the treatment, 9 patients (20%) had Gleason 3+3, and 3 patients had Gleason 7 disease (7%).

Regarding secondary treatments, 12 patients (11%) required adjuvant treatment for prostate cancer in this cohort. Of these, 10 (9%) required salvage whole gland treatment for progressive disease and 2 are taking androgen deprivation therapy for metastatic disease (see Table 3). Of these patients, 6 were intermediate risk with the others evenly distributed between high and low risk. Seven of these patients were treated by hemiablation. A further 12 patients required repeat focal HIFU to the prostate, 8 of these were from the intermediate risk group. In this cohort of patients there have been 4 patient deaths, none of which were related to prostate cancer.

Regarding side-effects, there was a 1% new use of pads (1 patient requiring 1 pad per day), 1.9% incidence of urethral stricture, 0% incidence of bladder neck contracture, 2.8% need for post-HIFU TURP, a 0% incidence of bowel injury, and new onset erectile dysfunction of 14% (see Supplementary Table 1).

DISCUSSION

This paper presents the results of a prospective study of 107 consecutive men treated for prostate cancer using

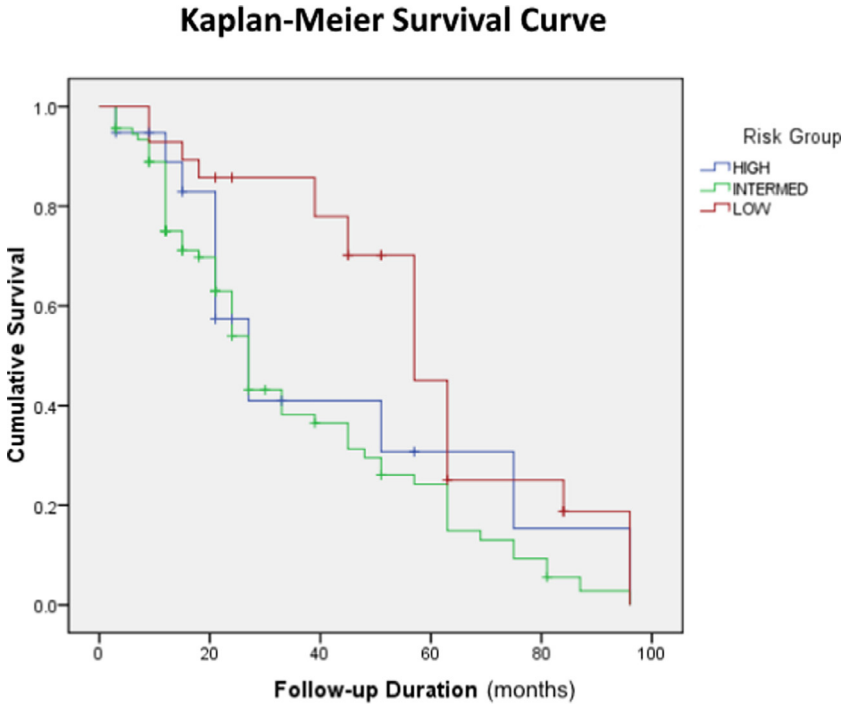

Figure 1. Kaplan-Meier analysis showing survivial from PSA failure for low intermediate and high-risk disease patients. (Color version available online.)

partial gland ablation, performed with HIFU, of whom 88% had intermediate/high risk disease and 69% had Gleason 7 or above disease. One hundred and seven of these men have been followed for at least 12 months, with a median follow-up of 30 months. It represents one of the largest single centre series of partial ablation gland ablation using HIFU, with one of the longest periods of follow-up, reported in the literature. The freedom from a secondary whole gland salvage procedure was better than 90% and freedom from any form of secondary procedure, including a redo focal procedure, was 75%. A total of 12% of men developed either contralateral disease, or near/in-field recurrence that warranted treatment, either focal or as part of a whole gland salvage procedure.

The main goal of a partial gland treatment is to reduce the side effects associated typically with whole gland therapy while maintaining a level of disease control close to that achieved with whole gland therapy. Compared to radical prostatectomy and radiotherapy, the frequency of side-effects such as erectile dysfunction and urinary incontience in this cohort of men was favourable. With prostatectomy, urinary incontinence requiring the use of pads occurs in high proportions of men in the immediate postoperative period (up to 3 months), can be as high as 46% at 6 months,[14] and decreases to a steady state of about 12%-15% by Year 2.[6,7,9] For radiation therapy, the acute incidence of urinary incontinence is very low but can increase to as much as 12% by Year 5.[15] Erectile dysfunction is very common regardless of therapy, occurring in greater than 50% of subjects in most studies.[15,16] Commonly ignored is the 100% incidence of loss of ejaculatory function with surgery (due to removal of the gland) and in excess of 50% with radiation therapy (due to damage to much of the gland).[17,18] Partial gland HIFU ablation has a side effect profile that is vastly superior to any whole gland therapy including whole gland HIFU—new onset urinary incontinence approaching 0%, preserved erectile function in 85% of men, practically 0% incidence of rectal complications, and preserved ejaculatory function in the vast majority of men.[4,19] This reduction in side effects is tied more to a reduction in the amount of gland targeted for treatment than to the specific technique used for the treatment.

Partial gland treatments must be compared against the current standard of care—whole gland therapy—in order to determine their role in the treatment of localized prostate cancer. Whole gland therapies such as prostatectomy produce 10-year CSS rates of 92%-100% with 10-year MFS rates of 89%-99%; radiation therapy and prostatectomy both produce BDFS at 5 years of 92%-100%, depending on risk stratification.[5,20] Whole gland HIFU produces similar medium-term disease control results. There are at least 3 independent centers in Europe that have reported 10-year CSS, a 10-year MFS, and a 5-year BDFS with HIFU equivalent to radical prostatectomy and radiation therapy.[6,7,21-22] In a comparative study of whole gland treatments for prostate cancer, Chiang and Liu reviewed patients treated with whole gland robotic radical prostatectomy, high dose rate brachytherapy, cryoablation, and HIFU for localized prostate cancer (100-160 men in each group).[8] PSA biochemical free survival was longer for HIFU compared to robotic radical prostatectomy (28 vs 22 months) as was the number of men who were salvage treatment free (70% vs 61%) and metastasis free (99% vs 95%).

Ahmed published the University College of London's first hemiablation series in 2011.[23] At 12-month follow-up, the mean PSA level decreased to 1.5 ± 1.3 ng/mL and 89% of patients had no histological evidence of cancer. The 2 patients (11.1%) with a positive biopsy at 6 months had marginal residual Gleason grade 3+3 disease of 1 mm.

Rischmann reported on the Crouzet group's experience in treating 111 patients with hemiablation using Ablatherm.[10] Of 101 patients with control biopsy, 96 (95%) and 94 (93%) had no CSD in the treated and contralateral lobes, respectively. The radical treatment-free survival rate at 2 years was 89%. Ganzer et al, Feijoo et al, and Van Vellthoven have all reported focal HIFU series also, with similar results.[19,24,25] The study reported here, on a predominately higher risk patient population treated with a single device produced an 8% rate of BCR, a 10% rate of clinically significant disease on biopsy for cause, and an overall freedom from progression to a whole gland salvage procedure of 93%.

Interpretation of these disease control results raises many questions, including what are the best measures of success or failure with focal therapy. Established PSA follow-up criteria used for whole-gland treatments, such as ASTRO, Phoenix, and Stuttgart, are difficult to apply after focal therapy as the untreated normal prostatic tissue will continue to secrete PSA. The more solid endpoints of metastases and death require over a decade of follow-up due to the long natural history of prostate cancer, making them prohibitively expensive and resource intensive. There is much debate as to how to measure success or failure of focal therapy and how to compare measures of success for focal therapy against whole gland interventions. There is growing belief that for focal therapy, progression to "salvage" treatment, regardless of the means used to identify men who need subsequent intervention, may be the best criterion. However, this criterion has not been applied universally when comparing focal HIFU to whole gland therapies such as prostatectomy and radiation therapy. In addition, it is unclear whether leaving a portion of the gland untreated will lead to poor oncologic outcomes arising from the untreated portion of the gland. Lastly, it is important to note that, for some men, a period of oncologic control followed by salvage treatment once the side-effects of more radical therapy are acceptable can be classed as a good outcome.

A shorter term measure of success is considered to be histologic evaluation following biopsy. However, this too carries issues regarding its own side-effect profile, and incidental findings of low risk contralateral disease. One of the main questions, in addition to what should be biopsied postfocal ablation, is what constitutes a treatment

failure. If clinically insignificant disease is not considered appropriate for treatment in the de novo setting, whether it is a treatment failure if clinically insignificant disease is found on post-HIFU biopsy in a patient treated originally for clinically significant disease is subject to debate. In addition, if clinically significant disease is found subsequently in the contralateral lobe whether that is a failure of the treatment, a failure of the diagnosis and management paradigm, or simply a new cancer is difficult to know. Thus, the International Multidisciplinary Consensus on Trial Design for Focal Therapy in Prostate Cancer decided that Gleason ≥ 7 on biopsy at 12 months post-treatment be regarded a failure of treatment in 2014. This group introduced the concept that a 1-time retreatment is acceptable for in-field recurrent or residual disease, or for new disease out-of-field. Moreover, they defined out-of-field clinically significant disease as a selection failure and not a treatment failure.

Guillaumier has applied these terminologies to HIFU registry data from the UK on 625 patients diagnosed with localised prostate cancer treated with focal HIFU.[26] Eight percent of men transitioned to a radical whole-gland therapy. The MFS and overall survival rates at 5 years were 97% and 99%, respectively. In total, 82% of patients who had satisfactory preoperative erection maintained their potency postoperatively. There were no major complications. A total of 20% of patients underwent a redo HIFU procedure in their cohort. These results are in-line with those reported here.

A repeat HIFU procedure to the same area, due to evidence of persistent disease on follow-up MRI, is not uncommon, occurring in 11% of patients in this report and up to 20% in other studies.[26,27] Repeat procedures may be necessary due to technical issues associated with the first treatment—target volume movement, failure to deliver adequate energy—as well as targeting errors. It is not uncommon for a repeat procedure to be performed on men with only clinically insignificant disease due to a patient's desire to be rid of all signs of cancer. How these additional HIFU procedures are viewed by clinicians and patients is, as yet, not reported fully in the literature. It is also clear that improvements in both technology and surgical skill can lead to a reduction in retreatment over time.[14] This learning curve effect is well known in surgery and we feel HIFU treatment in our centre has improved over time.

Studies are starting to appear comparing partial gland ablation to robotic prostatectomy in terms of disease control and side effect profiles. Albissini et al compared 55 men who underwent Ablatherm hemiablation to matched patients who underwent robotic prostatectomy that were found on final pathologic analysis to have unilateral disease and concluded that HIFU hemiablation is comparable to robotic prostatectomy in controlling localized unilateral prostate cancer but associated with significantly better functional outcomes.[27] Oncological control is important when comparing focal therapy and radical treatment, however, if a patient requires salvage prostatectomy following focal therapy, there have been concerns expressed over functional outcomes. Emerging research has shown that robotic surgery following focal therapy, for 82 patients in a multicentre cohort study, achieved high negative margin rates with modest additional treatment morbidity compared to patients treated initially with robotic prostatectomy.[28] This is important because it further strengthens the argument supporting the use of focal therapy in localised prostate cancer.

In conclusion, this series adds to the body of literature supporting the use of HIFU treatment for focal treatment of localized prostate cancer. The oncological control in the medium term was satisfactory and the side-effect profile in line with other publications. Prostate HIFU appears to be an efficacious treatment with low morbidity. In-time, long-term outcomes for prostate HIFU will be reported but, currently, series such as this advocate for this treatment in intermediate-risk disease. Randomised studies comparing focal treatment to whole gland radical therapy are required to allow overall acceptance of prostate HIFU as a treatment modality but the work done so far on this matter shows it is an option that should be considered for appropriate patients.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.06.043.

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EDITORIAL COMMENT

There is a lack of high-level evidence validating opinions how to best assess oncological outcome following partial gland ablation (PGA). Oncological outcome following PGA has been reported based on interval prostate specific antigen (PSA) and magnetic resonance imaging (MRI) testing, reflex or for cause biopsy, and rates of secondary treatments. There would be little disagreement that PGA achieved oncological control if men avoided whole gland treatment and did not develop metastasis or lethal disease. We will not know if PGA achieves these outcomes for decades. One of endpoints for expressing oncological control in the present study was avoidance of whole gland treatment. The FDA approves of this end point since it is clinically meaningful and measureable. With a median follow up of only 30 months, only 9% of men underwent went whole gland salvage treatment. So, may we conclude PGA with HIFU achieves intermediate oncological control? It is my experience that most men who are attracted to PGA will not undergo whole gland treatment under any circumstance .The surgeon can also heavily influence decisions how to manage in or out of field occurrence. For these reasons, I am hesitant to conclude that avoidance of whole gland salvage treatment at a median of 30 months indicates intermediate oncological control was achieved. The early validation studies of AS performed reflex biopsies at regular intervals to confirm oncological control. I strongly believe the absence of demonstrable disease should become the gold standard for assessing oncological control following PGA. Hopefully, we will ultimately demonstrate that PSA velocity or mpMRI individually, or in combination, can be reliable surrogates for oncological control. Identifying high volume GGG 1 or any Gleason pattern 4 in or out of field should be considered an oncological failure since this represents indication for treatment. Unfortunately, the authors did not prospectively mandate interval PSA and MRI testing and reflex biopsy in order to validate that noninvasive tests are reliable surrogates of oncological control.

Finally, it is imperative to set realistic expectations for oncological control following PGA. Approximately, 10%, 25%, 50%, and 65% of men with biopsy GGG 1, 2, 3, and 4 disease will develop biochemical recurrences at 8 years following RP, respectively. Therefore, we must anticipate and accept oncological failures following PGA. "Treatment failures" following RP are associated with modest rates of incontinence and high rates of sexual dysfunction. Oncological failures following PGA are associated with virtually no adverse functional outcomes. Men experiencing PGA treatment failures may opt for AS, secondary PGA, or whole gland treatment. As a surgeon who offers PGA to men with only clinically significant PCa, it is my conviction that while we may not cure the disease in some men, we will not compromise metastasis free and overall survival, providing we are vigilant in assessing and treating oncological failures in its early stages, The investigators did not discuss compliance with follow-up in their series. I believe the biggest challenge toward preventing metastatic and lethal disease following PGA will not be failure of treatment alone, but rather failure of vigilant follow-up.

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AUTHOR REPLY

We agree with the important points raised in this commentary. There is indeed a lack of evidence as to what constitutes optimal

follow-up following partial gland ablation (PGA). There can be no doubt that magnetic resonance imaging (MRI) has a significant part to play, and that it may indeed perform better than prostate specific antigen (PSA) profiles when it comes to predicting failure.[1] A total of 32% of the patients undergoing PGA using high-intensity focused ultrasound (HIFU) in this study over a 9-year period were treated within a National Institute for Health Research (NIHR) portfolio study and as such prostate biopsies were mandated. Those treated outside of a trial followed a similar protocol, with the exception of routine biopsy. All patients were followed closely post-treatment with regular PSA testing and interval MRI scanning following a protocol which is very similar to that used for our current active surveillance cohort.

Although imaging was central to our follow-up protocol, other biomarkers may prove to be of clinical benefit.[2] More research is also needed to validate PSA monitoring and MRI scanning as effective measures of oncological control.

Whilst some patients are indeed unwilling or reluctant to consider radical treatment, others are often given little or no information regarding PGA at the time of diagnosis. The ideal would be a balanced explanation of all relevant treatment options at the time of diagnosis with all the caveats that apply to an emerging tissue preserving approach. A lack of information will drive some men to social media and the internet leaving them vulnerable to misinterpretation.

The number of patients requiring whole gland treatment in this study is equivalent to several larger studies, referenced in the original text. In addition, though the data are not directly comparable, work by Marconi et al shows that men are willing to undergo salvage radical treatment if necessary.[3] Though this work also indicates uncertainty regarding oncological control following salvage RP post-PGA. In order to treat men with PGA then RP if required, we believe the preoperative consultations and consent process for focal HIFU PGA need to involve a discussion regarding future radical therapy if it becomes necessary, along with discussion of the alternatives to focal therapy from the outset.

We also feel that more realism is needed when comparing treatment outcomes, and failures, for both focal and radical therapies. The commentator reminds us all of the biochemical recurrence rates following radical prostatectomy. The outcomes for radical therapies, though based on more extensive and higher-level data, do not appear vastly superior to focal HIFU PGA. However, the author's position, which is similar to the commentator's, is that focal therapy represents an efficacious treatment with a low-side effect profile for appropriately selected patients.

Patients undergoing PGA do indeed require careful surveillance post-treatment and must understand from the outset the importance of adhering to follow-up regimes, and must be prepared to consider further PGA or salvage radical therapy as advised. In our experience patient motivation for follow-up is high with very few noncompliant.

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