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 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%, 23%, 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 vigilat follow-up.

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https://doi.org/10.1016/j.urology.2019.06.044


**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. 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. 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. 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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https://doi.org/10.1016/j.j.urology.2019.06.045