Detailing sexual outcomes after focal therapy for localised prostate cancer: a systematic review and meta-analysis

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Abstract

Context: Focal therapy has emerged as a promising option to treat well-selected men with localised prostate cancer while preserving healthy prostate tissue and key structures, such as the urethral sphincter and neurovascular bundles. However, how this tissue preservation may translate into improved outcomes, particularly into improved sexual outcomes, is still an active research field.

Objective: We conducted a systematic review and meta-analysis of the literature to summarise the existing evidence in order to provide patients with updated data on what to expect after treatment, and help identify gaps in current knowledge that may warrant future research.

Evidence acquisition: A systematic literature search was conducted on Medline, EMBASE, Scopus and Web of Science. The search strategy was defined using the 'litsearchr' function in R based on a preliminary "naïve" search using the following terms on Medline: (("focal therapy" OR

"focal treatment") AND ("prostate cancer") AND ("sexual function" OR "erectile function")). A total of 37 studies, comprising 2573 patients treated and 1992 with available sexual outcomes were included in the data synthesis.

Evidence synthesis: HIFU (n= 856, 43%) and cryotherapy (n=404, 20%) accounted for the highest number of patients analysed, while irreversible electroporation (n=137, 7%) was the least studied technique. The 5 item International Index of Erectile Function (IIEF-5) was the most frequently used questionnaire (26/37 studies), with completion rates ranging from 24-100% at 18-24 months. A significant decrease in IIEF-5 scores was noted at 3 months with an improvement at 6 and 12 months. Patients with an altered baseline sexual function were more likely to experience a significant postoperative decrease in erectile function scores. Continence rates (no pad use) ranged from 87.5 to 100%. Radical treatment rates ranged from 1.7% to 20.8%. The patient-reported outcomes (PRO) questionnaires used were not designed for a diverse population.

Conclusions: Focal therapy led to changes in erectile function in most cases under the significance threshold of the patient-reported outcomes questionnaires used. Patients should be counselled according to their baseline erectile function. More research is warranted to detail aspects other than erectile function. The early post-operative period appears key to study sexual changes after focal therapy, while only moderate changes are expected at 12 months.

Patient summary: We reviewed the published literature detailing the sexual consequences of focal therapy for localised prostate cancer using patient-reported outcomes questionnaires. Patients were likely to describe a significant decrease in their erectile function at 3 months, with an improvement noted at 6 and 12 months. The results obtained may not be reproducible in a more diverse population and further research is warranted to better study aspects other than erectile function.

1. Introduction

Focal therapy has emerged as a promising option to treat well-selected men with localised prostate cancer while preserving adjacent healthy prostate tissue and key structures, such as the urethral sphincter and neurovascular bundles. However, how this tissue preservation may translate into improved outcomes, particularly into improved sexual outcomes, is still an active research field. Early results with excellent potency preservation rates were often physician-reported. The patient-led EUPROMS study has recently shown us that there could be a significant gap between our physician-based idea of a good outcome and patient-reported outcomes (PROs) [1]. A large survey study including 934 men treated for localised prostate cancer found that significant sexual function bother was reported by 39% of men and strongly associated with treatment decision regret [2]. Another study linking PROs and decision regret confirmed that regret about the treatment choice (reported by 23% of patients) was more likely among patients with significant and enduring treatment-related symptoms [3]. How well we are able to inform patients on the possible post-operative outcomes has been shown of paramount importance to mitigate this treatment decision regret [4]. An international multidisciplinary consensus recently concluded that functional outcome assessment was a key component of focal therapy surveillance, but provided little guidance on how this endpoint should be achieved [5]. We conducted a systematic review and meta-analysis of the literature to summarise the existing evidence in order to help provide patients and professionals with updated data on what to expect after treatment, and help identify gaps in current knowledge that may warrant future research.

2. Evidence acquisition

2.1. Systematic literature search

A systematic literature search was conducted on Medline, EMBASE, Scopus and Web of Science. The search strategy was defined using the 'litsearchr' function in R software (R foundation, version 3.6.1) based on a preliminary "naïve" search using the following terms on Medline: ((“focal therapy” OR “focal treatment”) AND (“prostate cancer”) AND (“sexual function” OR “erectile function”)). The detailed Boolean search is

available as **Supplementary material**. Articles written in English only were considered. Reviews were excluded but their references were manually searched for additional references. The review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines and registered on PROSPERO (CRD42020165763).

2.2. Study methodology

Study selection was performed using the 'revtools' function in R, allowing for title and abstract screening. Study selection and data extraction were divided between a team of 4 (GF, AC, NRP, CP) to allow for double reading and checking of articles and data. Disagreements were solved by consensus and discussion with a fifth author (TY).

2.3. Risk of bias assessment

The following domains were assessed for risk of bias, using a modified IHE quality appraisal checklist: study objective, study design, study population, intervention and co-interventions, outcome measures, statistical analyses, follow-up and adverse events reporting, competing interests and sources of support [6]. It was chosen because it allowed for the evaluation of all studies using the same tool, considering all potential sources of bias in before-after case series. Each domain was rated at low, unclear or high risk of bias. Each study was independently assessed by 2 reviewers and disagreements solved by consensus. The risk of bias was rated as high for domains 5 (characteristics of the patients included) and 9 (additional interventions) if baseline erectile function (number of pre-operatively potent patients) and co-administration of erectile dysfunction medications (e.g., PDE5 inhibitors) were not clearly stated.

2.4. Data synthesis

The year of publication, design, number of patients treated, patients' characteristics (age, baseline sexual function, cancer characteristics), treatment energy type and volume, primary endpoint of the study, PRO tool used, completion rate and sexual function evolution, co-interventions (erectile dysfunction medication), urinary outcome and need for radical treatment were extracted for each study included. A qualitative synthesis was performed to summarise the results obtained for each review question. Median/mean scores obtained from PRO questionnaires were visually combined when possible (eg. IIEF-5 and SHIM, IIEF-6 and IIEF-15-Erectile Function Domain). We used 4 points as the minimal clinically important (significant) difference for IIEF-5 and IIEF-15-Erectile Function scores [7], and 12 points for EPIC-sexual domain scores [8]. IIEF-5 scores were combined into a meta-analysis to present postoperative erectile function at 3 months, 6 months and 12 months when mean/median scores and a dispersion measure (IQR, standard deviation or range) were available. Medians and IQRs were transformed into medians and SDs. Comprehensive meta-analysis (CMA) software Version 3.0 was used for the meta-analysis using a fixed-effect model with significance set at $p<0.05$.

3. Evidence synthesis

3.1. Literature search results

The literature search was first performed on 12/11/2019 and renewed on 6/03/2020. Overall, 901 records were identified from database search, and 18 through the manual search of the references included in literature reviews. After title and abstract screening, 164 full-texts were assessed for eligibility and 37 studies, comprising 2573 patients treated, among whom 1992 (77%) had available sexual outcomes and were included in the data synthesis (**Figure 1**).

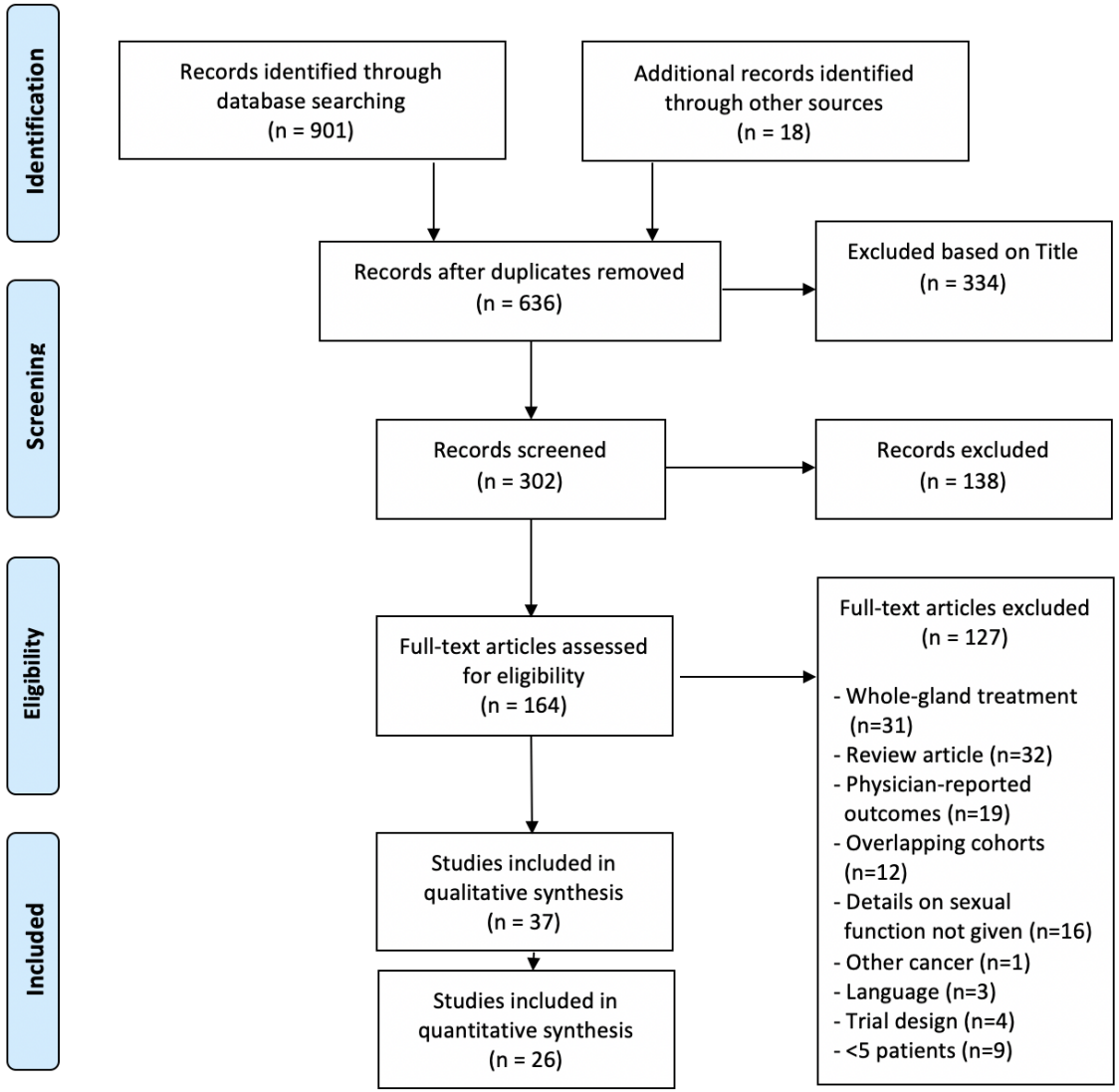

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 901)
Additional records identified through other sources (n = 18)
Records after duplicates removed (n = 636)
Excluded based on Title (n = 334)
Records screened (n = 302)
Records excluded (n = 138)
Full-text articles assessed for eligibility (n = 164)
Full-text articles excluded (n = 127)
- Whole-gland treatment (n=31)
- Review article (n=32)
- Physician-reported outcomes (n=19)
- Overlapping cohorts (n=12)
- Details on sexual function not given (n=16)
- Other cancer (n=1)
- Language (n=3)
- Trial design (n=4)
- <5 patients (n=9)
Studies included in qualitative synthesis (n = 37)
Studies included in quantitative synthesis (n = 26)

Figure 1. PRISMA flow diagram

3.2. Population and studies overview

Among the 37 studies included, 18 were prospective trials and 14 were based on prospectively gathered registries. Median number of patients with detailed sexual outcomes in each study was 30 (18-62). Median age varied from 56.5 to 71. Five studies provided data on patients' ethnicity, including a total of 336 treated patients, among whom 283 (84%) were white, 38 (11%) black, 7 (2%) Hispanic and 3 (1%) of Asian origin [9–13]. No details on ethnicity or sexuality were given for patients who answered PRO questionnaires. One study mentioned the use of questionnaires translated in a language other than English [14].

Median PSA ranged from 3.5 to 10.4 ng/ml. Out of the 2003 patients with available Gleason score data, 1012 (50%) had Gleason 3+3 disease and 973 (49%) Gleason 7 (3+4 n=749; 4+3 n=186; not detailed n=38). Median maximum cancer core length ranged from 1mm [15] to 8mm [16].

Self-reported scores at baseline defining baseline potency were clearly stated in 18/37 studies (49%) comprising 1028 patients. Using the threshold defined by each study, 719/1028 patients were pre-operatively potent with erections sufficient for penetration (70%). The risk of bias of the individual studies included is presented in the **Supplementary Figure 1**. Data extracted for each study are summarized in **Table 1**.


Risk of bias
D1 D2 D3 D4 D5 D6 D7 D8 D9 D10 D11 D12 D13 D14 D15 D16 D17
Study
Lindner 2009
Bahn 2012
Oto 2013
Barret 2013
Cosset 2013
Durand 2014
Barqawi 2014
Azzouzi 2015
Eggener 2016
Taneja 2016
Murray 2016
Natarajan 2016
Yap 2016
Feijoo 2016
Ting 2016
Chin 2016
Valerio 2016
Tay 2017
Srougi 2017
Natarajan 2017
Rischmann 2017
Valerio 2017
Chao 2018
Van den Bos 2018
Graff 2018
Von Hardenberg 2018
Ganzer 2018
Werneburg 2018
Shah 2019
Collettini 2019
Peters 2019
Walser 2019
Fischbach 2019
Sze 2019

Supplementary Figure 1. Risk of bias assessment of individual studies

3.3. Types of focal energy and data available

The various types of energies used, number of patients included and analysed are also detailed in **Table 1**. HIFU (n= 856, 43%) and cryotherapy (n=404, 20%) accounted for the highest number of patients analysed, while irreversible electroporation (n=137, 7%) was the least studied technique. All treatments, except for HIFU, were needle-based. The treatment template consisted either in hemiablation (n=953), or focal ablation (n=1039), with a mean/median treatment volume available in 12 studies and ranging from 2.2cc [17] to 23cc [18].

3.4. Types of PRO questionnaires and details collected

Of the 37 studies included, 26 used the 5 item International Index of Erectile Function (IIEF-5), otherwise known as the Sexual Health Inventory for Men (SHIM). Five used the 15 item International index of Erectile Function (IIEF-15), and 2 used the 6 item International Index of Erectile Function (IIEF-6), also known as the Erectile Function Domain which consists of questions 1-5 and 15 of the IIEF-15 (IIEF-15-EFD). Three studies used the Expanded Prostate Cancer Index Composite sexual domain (EPIC). One study used the Prostate Quality of Life Survey, a web-based tool based on the IIEF-6 for the evaluation of sexual function [19].

Of the five studies using IIEF-15, 3 presented results for the overall score and erectile function domain [16,20,21]. One study also reported detailed results on orgasmic function, intercourse satisfaction, sexual desire and overall satisfaction [22].

3.5. Acceptability of sexual follow-up

At baseline, the proportion of patients completing PRO questionnaires dedicated to their sexual function ranged from 47.5% [22] to 100% [20,23–25] . During follow-up, ranges evolved from 17%-92% at 6 months, 43-100% at 12 months and 24-100% at 18-24 months.

Overall, between 0% and 76% [26] of study populations did not complete all questionnaires. Most causes of dropout were not stated or simply described as "lost to follow-up". Reasons stated when reported included oncological unfavourable evolution (n=2) [14], PDE5 inhibitors use (n=11) [16,25], withdrawn consent (n=19) [11,14,27] and death due to unrelated causes [28].

3.6. Early and late erectile function evolution

All studies but one (n=36) [12] provided the detailed results of PRO questionnaires before and after treatment at various time points, ranging from 3 to 48 months.

Patient-reported sexual function using IIEF-5 was analysed for each focal therapy energy through a meta-analysis of the mean difference in IIEF-5 scores between baseline and 3 months (**Figure 2**), 6 months (**Figure 3**) and 12 months (**Figure 4**).

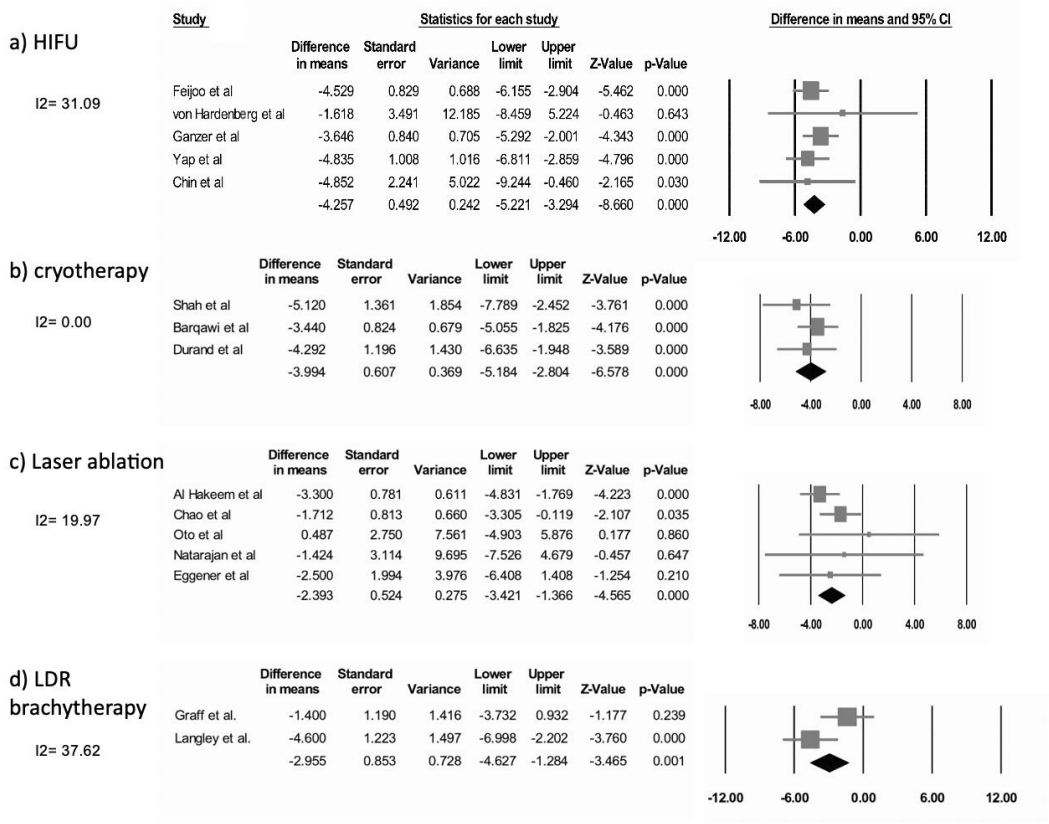
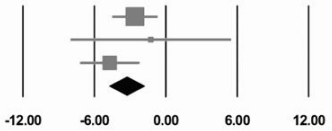


Figure 2: meta-analysis of the difference in mean IIEF-5 scores between baseline and 3 months

a) HIFU

I2= 43.13

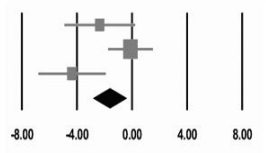
Study	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Yap et al	-2.593	0.971	0.944	-4.497	-0.689	-2.669	0.008
von Hardenberg et al	-1.258	3.432	11.781	-7.985	5.470	-0.366	0.714
Ganzer et al	-4.708	1.267	1.605	-7.191	-2.225	-3.716	0.000
	-3.275	0.752	0.566	-4.749	-1.800	-4.354	0.000



b) cryotherapy

I2= 67.74

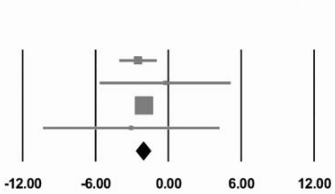
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Shah et al	-2.348	1.308	1.710	-4.911	0.216	-1.795	0.073
Barqawi et al	-0.110	0.827	0.683	-1.730	1.510	-0.133	0.894
Durand et al	-4.354	1.243	1.545	-6.790	-1.918	-3.503	0.000
	-1.615	0.609	0.371	-2.808	-0.421	-2.651	0.008



c) Laser ablation

I2= 0.00

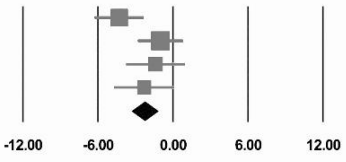
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Al Hakeem et al	-2.500	0.783	0.613	-4.035	-0.965	-3.193	0.001
Oto et al	-0.257	2.750	7.561	-5.646	5.133	-0.093	0.926
Walser et al	-2.000	0.342	0.117	-2.671	-1.329	-5.839	0.000
Natarajan et al	-3.054	3.703	13.709	-10.311	4.203	-0.825	0.409
	-2.064	0.311	0.097	-2.673	-1.455	-6.643	0.000



d) LDR brachytherapy

I2= 0.00

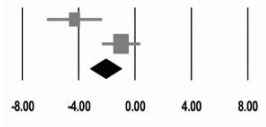
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Srougi et al.	-4.300	0.999	0.997	-6.257	-2.343	-4.306	0.000
Cosset et al.	-1.000	0.918	0.843	-2.799	0.799	-1.089	0.276
Graff et al.	-1.400	1.190	1.416	-3.732	0.932	-1.177	0.239
Langley et al.	-2.300	1.223	1.497	-4.698	0.098	-1.880	0.060
	-2.252	0.530	0.281	-3.290	-1.213	-4.251	0.000



e) HDR brachytherapy

I2= 80.77

	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Fischbach et al.	-4.300	0.999	0.997	-6.257	-2.343	-4.306	0.000
Peters et al.	-1.000	0.693	0.480	-2.358	0.358	-1.443	0.149
	-2.072	0.569	0.324	-3.188	-0.957	-3.641	0.000



f) Irreversible electroporation

I2= 74

	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Colletini et al	-2.713	1.024	1.049	-4.721	-0.705	-2.648	0.008
Valerio et al	1.000	1.592	2.536	-2.121	4.121	0.628	0.530
	-1.626	0.862	0.742	-3.315	0.062	-1.888	0.059

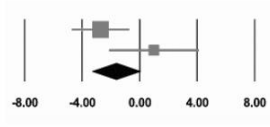
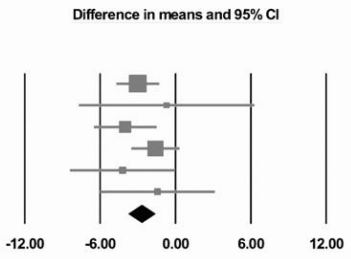


Figure 3: meta-analysis of the difference in mean IIEF-5 scores between baseline and 6 months

a) HIFU

I2= 27.29

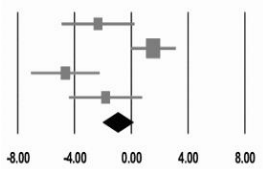
Study	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Lovegrove et al	-3.000	0.865	0.748	-4.695	-1.305	-3.469	0.001
von Hardenberg et al	-0.699	3.558	12.660	-7.672	6.275	-0.196	0.844
Ganzer et al	-4.000	1.268	1.607	-6.484	-1.516	-3.156	0.002
Yap et al	-1.593	0.972	0.944	-3.498	0.311	-1.640	0.101
Barret et al	-4.204	2.132	4.545	-8.382	-0.025	-1.972	0.049
Chin et al	-1.426	2.326	5.411	-5.985	3.133	-0.613	0.540
	-2.693	0.534	0.285	-3.740	-1.646	-5.040	0.000



b) cryotherapy

I2= 80.99

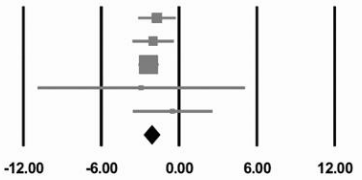
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Shah et al	-2.348	1.308	1.710	-4.911	0.216	-1.795	0.073
Barqawi et al	1.540	0.812	0.660	-0.052	3.132	1.896	0.058
Bahn et al.	-4.647	1.230	1.513	-7.058	-2.237	-3.779	0.000
Barret et al.	-1.815	1.311	1.717	-4.383	0.754	-1.385	0.166
	-0.947	0.547	0.299	-2.019	0.124	-1.732	0.083



c) Laser ablation

I2= 32.67

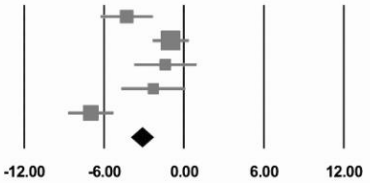
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Al Hakeem et al	-1.700	0.733	0.537	-3.137	-0.263	-2.319	0.020
Chao et al	-2.000	0.814	0.662	-3.595	-0.405	-2.457	0.014
Walser et al	-2.352	0.393	0.155	-3.123	-1.580	-5.976	0.000
Natarajan et al	-2.924	4.079	16.640	-10.919	5.071	-0.717	0.474
Eggener et al	-0.500	1.565	2.450	-3.568	2.568	-0.319	0.749
	-2.112	0.312	0.097	-2.723	-1.501	-6.778	0.000



d) LDR brachytherapy

I2= 0.00

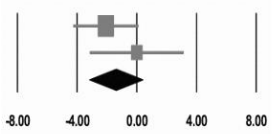
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Srougi et al.	-4.300	0.999	0.997	-6.257	-2.343	-4.306	0.000
Cosset et al.	-1.000	0.693	0.480	-2.358	0.358	-1.443	0.149
Graff et al.	-1.400	1.190	1.416	-3.732	0.932	-1.177	0.239
Langley et al.	-2.300	1.223	1.497	-4.698	0.098	-1.880	0.060
Barret et al	-7.000	0.869	0.755	-8.703	-5.297	-8.055	0.000
	-3.144	0.416	0.173	-3.959	-2.330	-7.563	0.000



e) Irreversible electroporation

I2= 15.21

	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Colletini et al	-2.070	1.117	1.248	-4.259	0.120	-1.852	0.064
Valerio et al	0.000	1.606	2.581	-3.149	3.149	0.000	1.000
	-1.395	0.917	0.841	-3.193	0.403	-1.521	0.128



f) Vascular targeted phototherapy

I2= 77.82

	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Barret et al.	-6.415	2.249	5.060	-10.824	-2.006	-2.852	0.004
Taneja et al.	0.206	1.946	3.786	-3.607	4.020	0.106	0.916
	-2.628	1.472	2.166	-5.512	0.257	-1.786	0.074

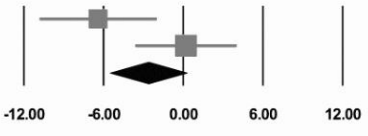


Figure 4: meta-analysis of the difference in mean IIEF-5 scores between baseline and 12 months

The evolution of PRO scores in the four studies using IIEF-15 scores [16,20–22], and the 3 studies reporting EPIC-sexual function scores [27,29,30] are presented graphically in **Figure 5**.

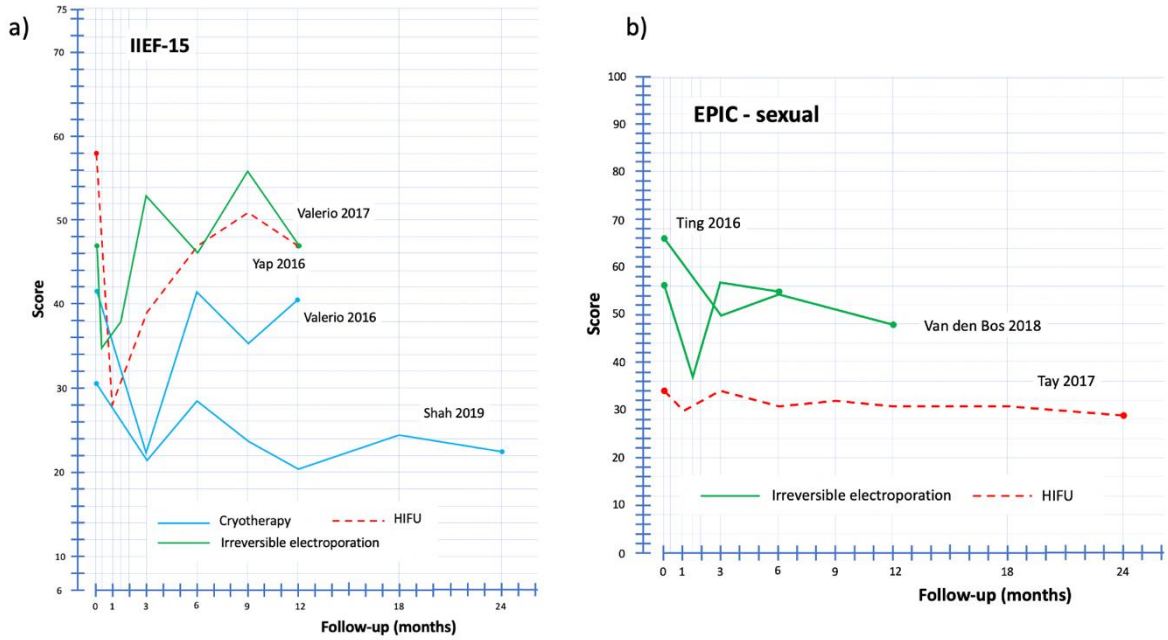


Figure 5. Evolution of mean/median IIEF-15 (a) and EPIC-sexual domain (b) scores

Lovegrove and colleagues also reported erectile dysfunction rates obtained from IIEF-5 questionnaires from a large cohort of patients (n=420) before and after primary or redo HIFU treatment. Baseline ED rates of 9.9% for primary and 12.8% for redo increased to 20.8% and 30.6% at 12 months before stabilising at 18.3% and 19% at 24 months, respectively [26].

Overall, among the 7 studies reporting erectile function of patients with no pre-operative erectile dysfunction (mean/median baseline IIEF-5 score ≥22) , including a total of 270 patients, only one study with 23 patients (8.5%) treated by focal VTP showed a significant decrease in patient-reported erectile function (median IIEF-5 decrease from 23 to 13) [31].
Nineteen studies included a total of 886 patients with mean/median IIEF-5 score showing mild ED at baseline (score between 17 and 21). Among these, scores showed a significant decrease (≥4 points) in 7 studies representing 424 patients (48%), including one prospective study using HDR brachytherapy and reporting a 13-point IIEF-5 score decrease among the 30 patients enrolled [32].

PDE5 inhibitors use before and after treatment was reported in 6/37 and 10/37 studies, respectively. At baseline, the proportion of patients treated with PDE5 inhibitors ranged from 7% [24] to 14% [14]. After treatment, the proportion increased in all studies but one [19], PDE5 inhibitors being used by 12.5% [21] to 47% [12] of patients .

3.7. Continence and need for radical treatment

Twenty-five studies provided data regarding post-operative continence. Using a definition of continence as no pad use, 17 studies reported no post-operative incontinence among the treated patients. Eight individual studies described post-operative incontinence rates ranging from 2.2% [27] to 12.5% [33].

The proportion of patients requiring radical treatment was available for 21 studies, and the mean/median follow-up was detailed in 11/21. The mean/median follow-up ranged between 3.7 [34] and 48 months [32]. Two studies reported no need for radical treatment with a short follow-up of up to 12 months [15,35]. In the other 19 studies, the radical treatment rate ranged from 1.7% [10] to 20.8% [33], with a rate of 16.7% in the study with the longest median follow-up (48 months) [32].

4. Discussion

The evidence displayed by this systematic review reveals several interesting aspects. Firstly, focal therapy led to changes in erectile function in most cases under the significance threshold of the patient-reported outcomes questionnaires used. However, patients should be counselled according to their baseline erectile function as most men with no erectile dysfunction at baseline were likely to have recovered their erectile function by 12 months, while men with even mild erectile dysfunction may experience a more significant and durable alteration of their erections. Secondly, most treatment effect on erectile function seems to appear shortly after treatment, in the 3 months post-treatment period, and the late recovery, after 12 months, appears to be modest. This is an important finding as it may help define future study protocols: an early time point (3 months) being key to analysing in-depth sexual consequences, while a 12-month time point can be used to assess recovery and erectile function preservation.

Thirdly, we need more evidence from studies looking at sexual function as a primary endpoint, as most studies focused and provided very detailed results on oncological outcomes, and by design did not consider confounding factors such as baseline potency and treatment by PDE5 inhibitors, while the results of PRO questionnaires were often found in the supplementary materials and proved more difficult to access.

Unsurprisingly, the IIEF-5 was the most widespread PRO questionnaire, and this allowed for a meta-analysis of the score reported after treatment with various energy sources. Of interest, it has originally been designed and validated in a population of men with erectile dysfunction of various origins, engaged in a stable relationship with a female partner for at least 6 months [36], and its measurement properties were recently questioned [37]. It also solely focuses on erectile function, and omits orgasmic, ejaculatory function, sexual desire or other masculinity/virility issues. Most of these domains are taken into account in the more thorough IIEF-15 questionnaire, used by 5 studies in this review. Unfortunately, the amount of patient-gathered data collected did not translate into more detailed study findings as the overall score and erectile-function domain were the only reported scores in all studies but one. Even more frustratingly, the details obtained in the latter appeared to be irrelevant because of very low baseline scores [22]. A previous study conducted by Li et al. had shown that it was possible to gather more in-depth descriptive results on sensitive issues such as penile length among patients treated by whole-gland HIFU and cryotherapy [38].

Although we weren't able to precisely gather the causes of dropout rates in each individual study, this review provides insight on the acceptability of such sexual follow-up on the short, medium and long-term. Depending on study design (clinical trial, prospective registry, retrospective), population size, length of follow-up and possibly other factors such as oncological and urinary outcomes, the rate of patients failing to complete all questionnaires was up to 76%. This is an important finding as it underlines the difficulties of conducting such a study on a large scale, but also possible issues with the PRO tools used and their perception by users. Guidelines are being issued to include a more diverse population into the design of new PRO tools and their validation, as well as new means of applying these tools, using for instance online questionnaires that the patient can fill outside the setting of a hospital/clinic visit.

Our results reveal a significant gap in knowledge on this highly topical subject, as previously highlighted for sexual outcomes after prostate cancer treatment in general [39]. Results obtained were collected from studies with good level of evidence, mostly of prospective design or clinical trials, but confounding factors such as baseline potency rate and PDE5 inhibitors use were often not reported. Although the small number of patients in many studies allowed for a thorough collection of outcomes, including PROs, it also exposes to a higher risk of selection bias. Many studies

were development studies, meaning that some degree of learning curve, either in the surgical technique or patient selection/treatment extent, has to be taken into account. The results obtained must be put in perspective with the profile of patients and cancers treated. Indeed, half of the patients had low-risk disease and would now probably be oriented towards active surveillance.

This review is not devoid of limitations. We chose to focus on sexual outcomes with the initial aim of reporting less frequently reported effects such as orgasmic and ejaculatory consequences, masculinity and virility issues, but the lack of published literature on these domains led us to consider patient-reported sexual outcomes instead. The studies included used a variety of PRO tools which prevented us from combining all data in the meta-analysis. Focal therapy regroups a variety of techniques, administered using a spectrum of tissue preservation templates, to preferentially treat different parts of the gland. Subsequently, patients treated form a heterogeneous group, as highlighted by the significant between-studies heterogeneity in the meta-analysis for several time points and energy types, making it more hazardous to draw definite conclusions. Reassuringly though, previous work showed that the treatment template did not significantly impact post-operative erectile function as long as at least one neurovascular bundle was preserved, which was the case in all techniques involved in this review [20].

5. Conclusion

Focal therapy led to changes in erectile function in most cases under the significance threshold of the patient-reported outcomes questionnaires used. Patients should be counselled according to their baseline erectile function as men with no baseline erectile dysfunction were more likely to recover. More research is warranted to detail aspects other than erectile function. The early post-operative period appears of interest to study detailed effects of focal therapy on aspects other than erectile function, while a 12-month time point is probably sufficient to assess post-operative recovery. Results were mostly obtained from studies with an oncological primary outcome, with highly-selected patients, and the drop-

out rate during follow-up was significant. Questionnaires used were not designed for a diverse population. More evidence is needed from studies looking at sexual function more broadly and individual expectations as primary endpoints.

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7. References

[1] EUPROMS study, available at https://www.europa-uomo.org/wp-content/uploads/2020/03/QOL-esou-dublin-template-Europa-Uomo-kopie.pdf, n.d.
[2] Hoffman RM, Lo M, Clark JA, Albertsen PC, Barry MJ, Goodman M, et al. Treatment Decision Regret Among Long-Term Survivors of Localized Prostate Cancer: Results From the Prostate Cancer Outcomes Study. J Clin Oncol 2017;35:2306–14. https://doi.org/10.1200/JCO.2016.70.6317.
[3] van Stam M-A, Aaronson NK, Bosch JLHR, Kieffer JM, van der Voort van Zyp JRN, Tillier CN, et al. Patient-reported Outcomes Following Treatment of Localised Prostate Cancer and Their Association with Regret About Treatment Choices. Eur Urol Oncol 2018. https://doi.org/10.1016/j.euo.2018.12.004.
[4] Christie DRH, Sharpley CF, Bitsika V. Why do patients regret their prostate cancer treatment? A systematic review of regret after treatment for localized prostate cancer. Psychooncology 2015;24:1002–11. https://doi.org/10.1002/pon.3776.
[5] Lebastchi AH, George AK, Polascik TJ, Coleman J, de la Rosette J, Turkbey B, et al. Standardized Nomenclature and Surveillance Methodologies After Focal Therapy and Partial Gland Ablation for Localized Prostate Cancer: An International Multidisciplinary Consensus. Eur Urol 2020. https://doi.org/10.1016/j.eururo.2020.05.018.
[6] Institute of Health Economics (IHE). Quality Appraisal of Case Series Studies Checklist. Edmonton (AB): Institute of Health Economics; 2014. Available from: http://www.ihe.ca/research-programs/rmd/cssqac/cssqac-about n.d.
[7] Rosen RC, Allen KR, Ni X, Araujo AB. Minimal Clinically Important Differences in the Erectile Function Domain of the International Index

of Erectile Function Scale. European Urology 2011;60:1010–6. https://doi.org/10.1016/j.eururo.2011.07.053.
[8] Skolarus TA, Dunn RL, Sanda MG, Chang P, Greenfield TK, Litwin MS, et al. Minimally important difference for the Expanded Prostate Cancer Index Composite Short Form. Urology 2015;85:101–5. https://doi.org/10.1016/j.urology.2014.08.044.
[9] Chao B, Llukani E, Lepor H. Two-year Outcomes Following Focal Laser Ablation of Localized Prostate Cancer. Eur Urol Oncol 2018;1:129–33. https://doi.org/10.1016/j.euo.2018.03.011.
[10] Walser E, Nance A, Ynalvez L, Yong S, Aoughsten JS, Eyzaguirre EJ, et al. Focal Laser Ablation of Prostate Cancer: Results in 120 Patients with Low- to Intermediate-Risk Disease. J Vasc Interv Radiol 2019;30:401-409.e2. https://doi.org/10.1016/j.jvir.2018.09.016.
[11] Taneja SS, Bennett J, Coleman J, Grubb R, Andriole G, Reiter RE, et al. Final Results of a Phase I/II Multicenter Trial of WST11 Vascular Targeted Photodynamic Therapy for Hemi-Ablation of the Prostate in Men with Unilateral Low Risk Prostate Cancer Performed in the United States. J Urol 2016;196:1096–104. https://doi.org/10.1016/j.juro.2016.05.113.
[12] Werneburg GT, Kongnyuy M, Halpern DM, Salcedo JM, Chen C, LeSueur A, et al. Effects of Focal vs Total Cryotherapy and Minimum Tumor Temperature on Patient-reported Quality of Life Compared With Active Surveillance in Patients With Prostate Cancer. Urology 2018;113:110–8. https://doi.org/10.1016/j.urology.2017.10.054.
[13] Chin JL, Billia M, Relle J, Roethke MC, Popeneciu IV, Kuru TH, et al. Magnetic Resonance Imaging-Guided Transurethral Ultrasound Ablation of Prostate Tissue in Patients with Localized Prostate Cancer: A Prospective Phase 1 Clinical Trial. Eur Urol 2016;70:447–55. https://doi.org/10.1016/j.eururo.2015.12.029.
[14] Ganzer R, Hadaschik B, Pahernik S, Koch D, Baumunk D, Kuru T, et al. Prospective Multicenter Phase II Study on Focal Therapy (Hemiablation) of the Prostate with High Intensity Focused Ultrasound. J Urol 2018;199:983–9. https://doi.org/10.1016/j.juro.2017.10.033.
[15] Oto A, Sethi I, Karczmar G, McNichols R, Ivancevic MK, Stadler WM, et al. MR imaging-guided focal laser ablation for prostate cancer: phase I trial. Radiology 2013;267:932–40. https://doi.org/10.1148/radiol.13121652.
[16] Valerio M, Shah TT, Shah P, Mccartan N, Emberton M, Arya M, et al. Magnetic resonance imaging-transrectal ultrasound fusion focal cryotherapy of the prostate: A prospective development study. Urol Oncol 2017;35:150.e1-150.e7. https://doi.org/10.1016/j.urolonc.2016.11.008.
[17] Lindner U, Weersink RA, Haider MA, Gertner MR, Davidson SRH, Atri M, et al. Image guided photothermal focal therapy for localized prostate cancer: phase I trial. J Urol 2009;182:1371–7. https://doi.org/10.1016/j.juro.2009.06.035.
[18] Azzouzi AR, Barret E, Bennet J, Moore C, Taneja S, Muir G, et al. TOOKAD® Soluble focal therapy: pooled analysis of three phase II studies assessing the minimally invasive ablation of localized prostate cancer. World J Urol 2015;33:945–53. https://doi.org/10.1007/s00345-015-1505-8.
[19] Murray KS, Ehdaie B, Musser J, Mashni J, Srimathveeravalli G, Durack JC, et al. Pilot Study to Assess Safety and Clinical Outcomes of Irreversible Electroporation for Partial Gland Ablation in Men with Prostate Cancer. J Urol 2016;196:883–90.

https://doi.org/10.1016/j.juro.2016.02.2986.
[20] Yap T, Ahmed HU, Hindley RG, Guillaumier S, McCartan N, Dickinson L, et al. The Effects of Focal Therapy for Prostate Cancer on Sexual Function: A Combined Analysis of Three Prospective Trials. Eur Urol 2016;69:844–51. https://doi.org/10.1016/j.eururo.2015.10.030.
[21] Valerio M, Dickinson L, Ali A, Ramachadran N, Donaldson I, Mccartan N, et al. Nanoknife Electroporation Ablation Trial: A Prospective Development Study Investigating Focal Irreversible Electroporation for Localized Prostate Cancer. J Urol 2017;197:647–54. https://doi.org/10.1016/j.juro.2016.09.091.
[22] Shah TT, Peters M, Miah S, Eldred-Evans D, Yap T, Hosking-Jervis F, et al. Assessment of Return to Baseline Urinary and Sexual Function Following Primary Focal Cryotherapy for Nonmetastatic Prostate Cancer. Eur Urol Focus 2019. https://doi.org/10.1016/j.euf.2019.09.004.
[23] Natarajan S, Jones TA, Priester AM, Geoghegan R, Lieu P, Delfin M, et al. Focal Laser Ablation of Prostate Cancer: Feasibility of Magnetic Resonance Imaging-Ultrasound Fusion for Guidance. J Urol 2017;198:839–47. https://doi.org/10.1016/j.juro.2017.04.017.
[24] Collettini F, Enders J, Stephan C, Fischer T, Baur ADJ, Penzkofer T, et al. Image-guided Irreversible Electroporation of Localized Prostate Cancer: Functional and Oncologic Outcomes. Radiology 2019;292:250–7. https://doi.org/10.1148/radiol.2019181987.
[25] Al-Hakeem Y, Raz O, Gacs Z, Maclean F, Varol C. Magnetic resonance image-guided focal laser ablation in clinically localized prostate cancer: safety and efficacy. ANZ J Surg 2019;89:1610–4. https://doi.org/10.1111/ans.15526.
[26] Lovegrove CE, Peters M, Guillaumier S, Arya M, Afzal N, Dudderidge T, et al. Evaluation of functional outcomes after a second focal high-intensity focused ultrasonography (HIFU) procedure in men with primary localized, non-metastatic prostate cancer: results from the HIFU Evaluation and Assessment of Treatment (HEAT) registry. BJU Int 2020. https://doi.org/10.1111/bju.15004.
[27] van den Bos W, Scheltema MJ, Siriwardana AR, Kalsbeek AMF, Thompson JE, Ting F, et al. Focal irreversible electroporation as primary treatment for localized prostate cancer. BJU Int 2018;121:716–24. https://doi.org/10.1111/bju.13983.
[28] Langley S, Uribe J, Uribe-Lewis S, Franklin A, Perna C, Horton A, et al. Hemi-ablative low-dose-rate prostate brachytherapy for unilateral localised prostate cancer. BJU Int 2020;125:383–90. https://doi.org/10.1111/bju.14948.
[29] Ting F, Tran M, Böhm M, Siriwardana A, Van Leeuwen PJ, Haynes AM, et al. Focal irreversible electroporation for prostate cancer: functional outcomes and short-term oncological control. Prostate Cancer Prostatic Dis 2016;19:46–52. https://doi.org/10.1038/pcan.2015.47.
[30] Tay KJ, Cheng CWS, Lau WKO, Khoo J, Thng CH, Kwek JW. Focal Therapy for Prostate Cancer with In-Bore MR-guided Focused Ultrasound: Two-Year Follow-up of a Phase I Trial-Complications and Functional Outcomes. Radiology 2017;285:620–8. https://doi.org/10.1148/radiol.2017161650.
[31] Barret E, Ahallal Y, Sanchez-Salas R, Galiano M, Cosset J-M, Validire P, et al. Morbidity of focal therapy in the treatment of localized prostate cancer. Eur Urol 2013;63:618–22. https://doi.org/10.1016/j.eururo.2012.11.057.
[32] Peters M, van Son MJ, Moerland MA, Kerkmeijer LGW, Eppinga WSC, Meijer RP, et al. MRI-Guided Ultrafocal HDR Brachytherapy for Localized Prostate Cancer: Median 4-Year Results of a feasibility study. Int J Radiat Oncol Biol Phys 2019;104:1045–53.

https://doi.org/10.1016/j.ijrobp.2019.03.032.
[33] von Hardenberg J, Westhoff N, Baumunk D, Hausmann D, Martini T, Marx A, et al. Prostate cancer treatment by the latest focal HIFU device with MRI/TRUS-fusion control biopsies: A prospective evaluation. Urol Oncol 2018;36:401.e1-401.e9. https://doi.org/10.1016/j.urolonc.2018.05.022.
[34] Bahn D, de Castro Abreu AL, Gill IS, Hung AJ, Silverman P, Gross ME, et al. Focal cryotherapy for clinically unilateral, low-intermediate risk prostate cancer in 73 men with a median follow-up of 3.7 years. Eur Urol 2012;62:55–63. https://doi.org/10.1016/j.eururo.2012.03.006.
[35] Cosset J-M, Cathelineau X, Wakil G, Pierrat N, Quenzer O, Prapotnich D, et al. Focal brachytherapy for selected low-risk prostate cancers: a pilot study. Brachytherapy 2013;12:331–7. https://doi.org/10.1016/j.brachy.2013.02.002.
[36] Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Peña BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res 1999;11:319–26. https://doi.org/10.1038/sj.ijir.3900472.
[37] Neijenhuijs KI, Holtmaat K, Aaronson NK, Holzner B, Terwee CB, Cuijpers P, et al. The International Index of Erectile Function (IIEF)—A Systematic Review of Measurement Properties. The Journal of Sexual Medicine 2019;16:1078–91. https://doi.org/10.1016/j.jsxm.2019.04.010.
[38] Li L-Y, Lin Z, Yang M, Gao X, Xia T-L, Ding T. Comparison of penile size and erectile function after high-intensity focused ultrasound and targeted cryoablation for localized prostate cancer: a prospective pilot study. J Sex Med 2010;7:3135–42. https://doi.org/10.1111/j.1743-6109.2010.01751.x.
[39] Lovegrove CE, Ficarra V, Montorsi F, N'Dow J, Salonia A, Minhas S. Sexual function outcomes following interventions for prostate cancer: are contemporary reports on functional outcomes misleading? Int J Impot Res 2019. https://doi.org/10.1038/s41443-019-0220-1.

Study	**Year**	**Focal energy type**	**Template (mean/median volume treated – cc/ablation area diameter-mm)**	**Patients treated/evaluated (sexual outcomes) N**	**Acceptability (PRO questionnaires completed at baseline and follow-up) N (time point)**	**Number potent patients (pre-op)**	**Age** median(IQR) *mean (SD)* [range]	**Sexual outcome evaluation tool**	**Evaluation time points (months)**	**Results (PRO)** median (IQR) *mean (SD)* [range]	**Post-op ED medication N (time point)**	**Incontinence (last follow-up) N (%)**	**Need for radical treatment N (%)**	**Follow-up (months)**
Lindner	2009	Laser ablation	Focal (2.2cc)	12/12	NR	NR	56.5[51-62]	IIEF-5	0/1/3/6	22/21/20/23	NR	0/12 (0)	2/12 (17)	NR
Bahn	2012	Cryotherapy	Hemiablation	73/63	63/73 (0)	42/63	64 [47-79]	IIEF-5	0/12/24	22 [13-25]/17 [5-24]/19 [5-25]	NR	0/70 (0)	4/70 (5.7)	3.7 [1-8.5]
Oto	2013	Laser ablation	Focal (NR)	9/9	NR	6/9	61 [52-77]	SHIM	0/1/3/6	23 (11-24)/24 (19-24)/22 (13-24)/22 (12-23)	NR	NR	0/9 (0)	NR
Barret	2013	Cryotherapy LDR Brachytherapy VTP HIFU	Hemiablation	50/50 12/12 23/23 21/21	NR	NR	66.5 (61-73)	IIEF-5	0/12	19 (9–25)/ 14 (8–25) 21 (10–25)/ 14 (8–24) 23 (17–25) /13 (7–25) 20 (15–25)/ 14 (8–25)	NR	0/106 (0)	NR	9 (6-15)
Cosset	2013	LDR Brachytherapy	Focal (14cc)	21/21	NR	NR	62.3 [56-74]	IIEF-5	0/2/6/12	20.1 [5-25]/18.6 [5-25]/19.1 [5-25]/19.8 [5-25]	NR	0/21 (0)	0/21 (0)	NR
Durand	2014	Cryotherapy	Hemiablation	64/48	29/48 (0) 8/48 (6)	37/48	*66.6 [50.4-77.1]*	IIEF-5	0/3/6	17 (7-21)/12 (3-17)/13 (2-17)	NR	0/48 (0)	3/48 (6.2)	13.2 (7.4-26.5)
Barqawi	2014	Cryotherapy	Focal (NR)	62/62	NR	NR	*60.5 (6.8)*	SHIM	0/3/6/12/24	*16.1 (8.6)/12.7 (8.1)/16 (8.1)/17.6 (7.8)/19.1 (5.9)*	NR	0/62	2/62 3.2)	28 (26-31)
Azzouzi	2015	VTP	Hemiablation (23cc)	117/117	NR	NR	*62.2*	IIEF-5	0/1/3/6	*19.4/12.9/15.1/15.3*	NR	NR	NR	NR
Eggener	2016	Laser ablation	Focal (15mm)	27/27	NR	NR	62	SHIM	0/1/3/12	21.5 (10.5)/19 (16.5)/19 (14.5)/21 (10.5)	NR	1/27 (3.7)	1/27 (3.7)	NR
Taneja	2016	VTP	Hemiablation	30/28	28/30 (0)	NR	63 (47-74)	IIEF-5	0/1/3/6/12	18 (10-26)/14 (5-22)/15 (7-23)/15 (8-23)/14 (5/23)	NR	2/30 (6.7)	NR	NR
Murray	2016	Irreversible electroporation	Focal (NR)	25/22	22/25 (0) 16/25 (6) 17/25 (12)	13/22	63 (59-68)	PQLS (IIEF-6)	0/6/12	18.6/16.2/21.1	2/22 (0) 2/22 (12)	2/22 (9)	3/25 (12)	10.9
Natarajan	2016	Laser ablation	Focal (3cc)	8/8	NR	NR	63 (60-66)	SHIM	0/6	19.5/20	NR	0/8 (0)	NR	NR
Yap	2016	HIFU	Hemiablation n=20 Focal (NR) n=98	118/118	118/118 (0) 112/118 (12)	NR	63 (52-70)	IIEF-15 IIEF-15-EFD	0/1/3/6/9/12	58 (32-67)/28 (13-50)/39 (21-58)/47 (26-61)/51 (26-64)/47 (28-62) 23 (11-28)/9 (3-22)/15 (6-26)/19 (8-27)/20 (9-29)/20 (9-28)	12/118 (0) 35/118 (3) 51/118 (6) 44/118 (12)	NR	NR	NR
Feijoo	2016	HIFU	Hemiablation	71/67	67/71 (0)	21/67	*70.2 (6.8)*	IIEF-5	0/3	20 (15-23)/16 (8-20.5)	NR	0/67 (0)	NR	12 (6-50)
Ting	2016	Irreversible electroporation	Focal (NR)	32/25	18/25 (6)	NR	67 (60-71)	EPIC	0/1.5/3/6	56 (51-75)/37 (29-63)/57 (31-65)/55 (34-69)	NR	0/25 (0)	1/25 (4)	8

Chin	2016	Transurethral HIFU (TULSA)	Focal (NR)	30/30	29/30 (12)	21/30	69 (67-71)	IIEF-15-EFD	0/1/3/6/12	13 (6-28)/7 (2-12)/11 (4-18)/11 (4-19)/13 (5-25)	NR	0/30 (0)	2/30 (6.7)	NR
Valerio	2016	Cryotherapy	Focal (NR)	18/18	13/18 (12)	NR	68 (65-73)	IIEF-15	0/3/6/9/12	41 (12-59)/22 (16-39)/41 (32-47)/35 (21-52)/40 (30-57)	2/18 (0) 5/18 (12)	NR	NR	NR
Tay	2017	HIFU	Focal (NR)	14/14	12/14 (24)	NR	*62.8 (4.6)*	EPIC	0/1/3/6/9/12/18/24	34 (29-36)/30 (17-37)/34 (29-37)/31 (26-35)/32 (27-38)/31 (26-37)/31 (26-39)/29 (25-35)	NR	NR	NR	NR
Srougi	2017	LDR Brachytherapy Base n=13 Apex n=28	 Focal (14.1) Focal (11.9)	47/41	30/41 (0) 33/41 (12)	NR	63 (50-79)	IIEF-5	0/6/12/24	 18 (6.9)/16.3 (5.6)/16.2 (6.3)/16.5 (7.4) 19 (7.6)/14.7 (8.7)/16.5 (7.5)/17 (7.7)	NR	NR	NR	NR
Natarajan	2017	Laser ablation	Focal (4.3)	10/10	10/10 (0,3) 9/10 (6,9) 8/10 (12)	4/10	65	IIEF-5	0/7d/1/3/6/9/12	15.5 (9.5-24)/14 (3-25)/ 8(2-25)/15 (4.5-22)/13 (4-23)/12 (3-24)/13.5 (3-24)	NR	NR	NR	NR
Rischmann	2017	HIFU	Hemiablation (16.1)	111/111	NR	51/111	64.9 (61-69)	IIEF-5	0/12	20 (13-24)/19 (9/22)	NR	3/102 (2.9)	13/111 (11.7)	*30.4 (14.1)*
Valerio	2017	Irreversible electroporation	Focal (NR)	19/16	16/19 (0) 16/19 (12)	12/16	60 (53-66)	IIEF-15	0/7d/1.5/3/6/9/12	47 (28-63)/35 (20-62)/38 (21-52)/53 (25-60)/46 (36-56)/56 (34-63)/47 (33-58)	2/16	0/19 (0)	2/19 (10.5)	NR
Chao	2018	Laser ablation	Focal (NR)	34/34	32/34 (12)	NR	69 (52-88)	SHIM	0/12	22 (20-24)/20 (16-24)	NR	0/34 (0)	NR	NR
Van den Bos	2018	Irreversible electroporation	Focal (NR)	63/44	44/63 (0) 19/44 (12)	31/44	67 (61-71)	EPIC	0/3/6/12	66 (47-85)/50 (27-75)/54 (29-72)/48 (15-77)	NR	1/45 (2.2)	3/45 (6.7)	NR
Graff	2018	LDR Brachytherapy	Focal (5.5)	17/17	NR	NR	66 (59-69)	IIEF-5	0/1/3/6/12	17 (14-21)/17 (13-21)/16 (11-20)/16 (12-20)/16 (12-20)	NR	0/17 (0)	1/17 (5.9)	NR
Von Hardenberg	2018	HIFU	Focal (6.81)	24/24	22/24 (12)	9/24	70 (52-78)	IIEF-5	0/3/6/12	19.5 [0-25]/15 [0-24]/15 [1-24]/17 [0-25]	3/9 (12)	3/24 (12.5)	5/24 (20.8)	*18.4 (5.8)*
Ganzer	2018	HIFU	Hemiablation	54/51	51/54 (0)	30/51	*63.4 (8.3)*	IIEF-5	0/3/6/9/12	19 (14-22)/15 (9-20)/15 (5-21)/15 (5-21)/15 (6-22)	7/51 (0) 12/51 (12)	3/51 (5.9)	10/51 (19.6)	*17.4 (4.5)*
Werneburg	2018	Cryotherapy	Hemiablation	129/89	89/129 (0)	NR	69	IIEF-15 EPIC	NR	NR	42/89	NR	NR	30
Shah	2019	Cryotherapy	Focal (NR)	122/58	58/122 (0)	NR	69 (65-73)	IIEF-15 IIEF-15-EFD	0/3/6/9/12/18/24	31 (14-56)/22 (13-34)/29 (14-46)/24 (15-51)/21 (8-38)/25 (18-48)/23 (11-28) 8 (2-20)/5 (1-9)/6 (1-16)/7 (2-19)/4 (1-12)/8 (2-17)/5 (2-11)	5/58 (0) 19/58 (12)	NR	NR	NR
Collettini	2019	Irreversible electroporation	Focal (NR)	30/30	30/30 (0) 29/29 (12) 12/12 (24)	25/30	65.5 (60-68.8)	IIEF-5	0/6/12/24	21 (16-24)/19 (12-22)/20 (12-23)/22.5 (18.5-25)	2/30 (0) 6/30 (6) 3/29 (12)	1/29 (3.4)	2/30 (6.7)	20 (14-29)
Peters	2019	HDR brachytherapy	Focal (NR)	30/30	30/30 (0) 25/30 (1) 24/30 (12) 16/30 (48)	16/30	71 (68-73)	IIEF-5	0/1/3/6/9/12/18/24/36/48	19 (5-22)/17(4-22)/9 (4-18)/6 (4-17)/7 (4-16)/6 (3-19)/8 (3-16)/5 (4-18)/7 (4-20)/6 (3-20)	NR	NR	5/30 (16.7)	48

Walser	2019	Laser ablation	Hemiablation	120/120	NR	NR	64 [45-86]	SHIM	0/6/12/24	24 (20-25)/22 (17-24)/22 (16-24)/22 (16-24)	NR	0/120 (0)	2/120 (1.7)	34 (17-55)
Fischbach	2019	HDR brachytherapy	Focal (4.67)	9/9	7/9 (6)	6/9	65 (61-67)	IIEF-6	0/6	28 (21-30)/27 (26-30)	NR	NR	NR	15
Sze	2019	Cryotherapy	Focal (NR)	17/16	16/17 (0)	3/16	67	IIEF-5	0/12	19.5/19	NR	0/16 (0)	NR	15 (13-17)
Al Hakeem	2019	Laser ablation	Focal (2.4)	49/49	49/49 (0) 44/49 (3) 45/49 (6) 40/49 (12,18)	NR	63 [51-73]	SHIM	0/1/3/6/12/18	*19.3/15.2/16/16.8/17.6/18.3*	9/49	0/49 (0)	6/49 (12.2)	18
Lovegrove	2020	HIFU primary HIFU redo	Focal (NR) n=315 Hemiablation n=105	654/355 167/65	355/654 (0) 161/654 (24) 65/167 (0) 34/167 (24)	320/355 57/65	*66.4 (7.3)* *65.6 (7)*	IIEF-5	0/12/24	*14 (9)/11 (9)/13 (10)*	NR	NR (4.7)	NR	64.9 (41.9-78.9) 72.5 (65.8-91)
Langley	2020	LDR Brachytherapy	Hemiablation	30/28	28/30 (0) 24/30 (24)	15/28	*65.6 (7.6)*	IIEF-5	0/3/6/12/18/24	*13.7 (8.7)/9.1 (8.6)/11.4 (8.6)/11.2 (9.5)/12.1 (9.9)/12.6 (9.9)*	NR	NR	1/26 (3.8)	NR

Table 1. Detailed data extracted from each study (LDR: Low Dose Rate; HDR: High Dose Rate; NR-not reported; results are presented as medians (IQR)[range] or *means (SD)*