



# Prostate cancer treatments

Are high-intensity focused ultrasound (HIFU), irreversible electroporation (IRE) and cryotherapy recommended treatments in prostate cancer?

This review covers three distinct populations of interest: Localised cancers, Metastasis or secondary cancers and Recurrent cancers



## Summary and recommendations

### Localised cancer

The current evidence for HIFU, Irreversible Electroporation (IRE) and cryotherapy in Prostate Cancer is currently unproven (Amber AXA Health Patient Safety Rating). Specifically, the treatments are listed by NICE as in-trial only (see recommendations 1.3.26 and 1.3.31).

A NICE review was updated in May 2019 and recommended not offering high-intensity focused ultrasound [HIFU] and cryotherapy to people with localised prostate cancer, other than in the context of controlled clinical trials comparing their use with established interventions.

The NICE recommendations are backed up by The European Association of Urology (EAU) who recommended that whole gland treatment (such as cryotherapy, high-intensity focused ultrasound [HIFU], etc.) or focal treatment should be offered within a clinical trial setting.

### Metastasis or secondary cancers

The current evidence does not support HIFU, Irreversible Electroporation (IRE) and cryotherapy in metastatic or secondary prostate cancer (Amber AXA Health Patient Safety Rating).

### Recurrent cancer

Minimally invasive options offer promising results in terms of biochemical control in local recurrence, however, there is an absence of high quality trials and comparative studies that make it difficult to establish which method is the safest and most effective. (Amber AXA Health Patient Safety Rating).

Patient  
safety  
rating:  
amber

Recent updated searches show an absence of high quality and comparative studies that make it difficult to establish effectiveness. There are several ongoing trials that have either completed or will complete in the next three years, meaning this guidance should be kept under review as new evidence is likely to emerge prior to any NICE update.



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## Localised cancer

### Guidelines

The 2019 NICE guideline on [Prostate Cancer](#) reported on HIFU and cryotherapy, stating:

*“1.3.26 Do not offer high-intensity focused ultrasound and cryotherapy to people with localised prostate cancer, other than in the context of controlled clinical trials comparing their use with established interventions.”*

The guideline does not report on IRE. However, there is a separate, 2016 [Interventional Procedures guidance](#) which states (for prostate cancer generally, not specifically localised):

*“1.1 Current evidence on the safety and efficacy of irreversible electroporation for treating prostate cancer is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. Studies should include randomised controlled trials comparing the procedure with current standards of care. They should report details of patient selection and short- and long-term outcomes, including patient-reported outcomes and the effect on any future prostate surgery.”*

More recently, 2020, the European Association of Urology (EAU) published a [guideline on prostate cancer](#). For low--risk localised disease they state:

*“Only offer whole gland treatment (such as cryotherapy, high-intensity focused ultrasound, etc.) or focal treatment within a clinical trial setting or well-designed prospective cohort study.”*

For intermediate-risk disease:

*“Only offer whole-gland ablative therapy (such as cryotherapy, high-intensity focused ultrasound, etc.) or focal ablative therapy for intermediate-risk disease within a clinical trial setting or well-designed prospective cohort study.”*

And, for high-risk localised disease:

*“Do not offer either whole gland or focal therapy to high-risk patients.”* (which includes HIFU, cryotherapy and electroporation).

### AHRQ

Have just published [Therapies for Clinically Localized Prostate Cancer](#) which reports the following:

*"For these modalities, often targeted to lower risk focal CLPC, including cryotherapy, laser ablation, and high-intensity focused ultrasound, evidence was insufficient."*

*"For many important comparisons, especially as related to newer treatment modalities such as HIFU or photodynamic therapy, we found no evidence for oncological outcomes."*

### Systematic reviews

We searched for systematic reviews, via PubMed and Trip, for each intervention published in 2020 (overlapping the EAU guideline).

[The primary treatment of prostate cancer with high-intensity focused ultrasound: A systematic review and meta-analysis](#). Medicine (Baltimore). 2020 Oct

### Conclusions

Early evidence suggested the partial-gland HIFU was safer than whole-gland HIFU, and they had similar oncological outcomes. More prospective randomised controlled trials of whole-gland and partial-gland HIFU for PCa was needed.

We found no 2020 systematic reviews for electroporation or cryotherapy.



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### Metastasis or secondary cancers

#### Guidelines

The NICE guideline does not mention any of the therapies in relation to metastatic prostate cancer (section 1.5) which is the same in the EAU guidance. As neither guideline looked at these interventions we looked for more global guidelines and found recent guidance from [Canada](#) and [Australia](#). Both discuss metastatic disease, and neither report on either of the three interventions of interest.

#### Systematic Reviews

Given the lack of mention of the interventions in the main guidelines we looked for any systematic reviews conducted in the last five years in the three interventions and found none.

#### Randomised Controlled Trials

Given the lack of mention of the interventions in the main guidelines or systematic reviews we looked for any RCTs in the three interventions and found none.

### Recurrent cancer

#### Guidelines

The NICE guideline does not discuss follow-up after local treatment while the EAU makes the following recommendation in the section 'Guidelines for second-line therapy after treatment with curative intent':

*"Only offer salvage high intensity focused ultrasound, salvage cryosurgical ablation and salvage brachytherapy to patients with proven local recurrence within a clinical trial setting or well-designed prospective cohort study."*

#### Systematic reviews

[Minimally invasive strategies for the treatment of prostate cancer recurrence after radiation therapy: a systematic review](#). Minerva Urol Nefrol. 2020 Aug

Conclusions: Minimally invasive therapeutic options offer promising results in terms of biochemical control in the local recurrence setting. Unfortunately, the absence of high quality and comparative studies makes it difficult to establish which method is the best in terms of oncological and safety outcomes.

[Nonsurgical Salvage Local Therapies for Radiorecurrent Prostate Cancer: A Systematic Review and Meta-analysis](#). Eur Urol Oncol. 2020 Apr

Conclusions: Nonsurgical therapeutic options, especially BT, showed good outcomes in terms of biochemical control and tolerability in the local recurrence setting.

[A systematic review of salvage focal therapies for localised non-metastatic radiorecurrent prostate cancer](#). Transl Androl Urol. 2020 Jun

Synthesis: A total of 64 case-series studies were included, corresponding to a cohort of 5585 patients. The modified Delphi checklist evidenced high methodological quality overall (mean quality score of 80.6%). Biochemical control rates were lowest for patients treated with HIFU (58%, 95% confidence interval [CI] 47-68%) and highest for patients treated with BT (69%, 95% CI 62-76%) and EBRT (69%, 95% CI 53-83%). The lowest prevalence of incontinence was for patients treated with BT (3%, 95% CI 0-6%; I<sup>2</sup>=63.4%) and the highest was among patients treated with HIFU (28%, 95% CI 19-38%; I<sup>2</sup>=89.7%).



**Health**

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## **Prostate cancer treatments**

### **Ongoing clinical trials**

Searched via [clinicaltrials.gov](https://clinicaltrials.gov)

HIFU – [43 results](#) (Trials.Gov link)

- The majority are either finished, recruiting or not active. Six trials are active and not recruiting.
- These have a variety of completion dates up to 2022.
- 11 completed interventional trials and none have results posted.

Cryotherapy – [34 results](#) (Trials.Gov link)

- The majority are either finished, recruiting or not active.
- These have a variety of completion dates up to 2022.
- 11 completed interventional trials and two have results posted.

Irreversible electroporation – [11 results](#) (Trials.Gov link)

- The majority are either finished, recruiting or not active.
- The one ongoing trial - Multi-Center Randomized Clinical Trial Irreversible Electroporation for the Ablation of Localized Prostate Cancer - has a primary completion date of this year and a “Estimated Study Completion Date” of 2025.
- 3 completed trials and none have results posted.