

# Irreversible Electroporation for Prostate Cancer

Subjects: Oncology

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By focusing treatment on a specific area of the prostate gland, the aim of focal therapy is to achieve similar oncological outcomes to radical treatment while preserving functional outcomes and decreasing the rates of adverse effects. Irreversible electroporation (IRE) is a novel focal therapy modality which utilises pulsatile electrical currents to ablate tissue. Animal and human models have been used to prove that IRE can induce cell death whilst preserving important surrounding structures.

Keywords: prostate cancer ; irreversible electroporation ; focal therapy ; surgery

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## 1. Overview

Although it can be lethal in its advanced stage, prostate cancer can be effectively treated when it is localised. Traditionally, radical prostatectomy (RP) or radiotherapy (RT) were used to treat all men with localised prostate cancer; however, this has significant risks of post-treatment side effects. Focal therapy has emerged as a potential form of treatment that can achieve similar oncological outcomes to radical treatment while preserving functional outcomes and decreasing rates of adverse effects. Irreversible electroporation (IRE) is one such form of focal therapy which utilises pulsatile electrical currents to ablate tissue. This modality of treatment is still in an early research phase, with studies showing that IRE is a safe procedure that can offer good short-term oncological outcomes whilst carrying a lower risk of poor functional outcomes. We believe that based on these results, future well-designed clinical trials are warranted to truly assess its efficacy in treating men with localised prostate cancer.

## 2. Prostate cancer

Prostate cancer continues to be one of the most commonly diagnosed cancers in men and a leading cause of cancer deaths in males worldwide <sup>[1]</sup>. Although it can be lethal in its advanced stage, prostate cancer can be effectively treated when it is localised. Traditionally, radical prostatectomy (RP) or radiotherapy (RT) were used to treat all men with localised prostate cancer regardless of their risk. However, notwithstanding their improved overall survival benefits, RP and RT have significant risks of post-treatment side effects; the two most common being urinary incontinence (UI) and erectile dysfunction (ED).

The last decade has seen a change in management for very low and low risk prostate cancer and an increasing interest in new techniques for the treatment of intermediate risk prostate cancer. Very low and low risk prostate cancer has an unlikely chance of metastasis and a very low risk of mortality <sup>[1]</sup>. As such, guidelines now recommend treatment with active surveillance to delay or mitigate the need for RP or RT <sup>[2]</sup>. Similarly, some evidence suggests that intermediate risk prostate cancer can have oncological outcomes close to that of low risk prostate cancer <sup>[3]</sup>. However, the risk of metastasis is still relevant and warrants some form of treatment. Different forms of focal therapy to the prostate gland are currently being trialled for these men.

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The mechanism in which IRE does this is through the destabilisation of the cell membrane, causing the alteration of membrane shape and the formation of nanopores. The excessive permeability of these cells disrupts the osmotic balance, leading to irreversible damage and the process of apoptosis <sup>[5]</sup>. This technique has now been refined to administer electrical pulses at levels to prompt cell death whilst keeping the procedure below harmful thermal thresholds <sup>[4]</sup>. For important structures such as blood vessels, IRE has been shown to decrease smooth muscle cells but maintain the

connective tissue matrix [6]. Thus, it has been used effectively in liver lesions where damage to bile ducts and hepatic vessels are lethal [7,8]. For men with prostate cancer, preservation of the neurovascular bundles adjacent to the gland can result in preservation of continence and erectile function, therefore increasing quality of life.

Initial trials for localised prostate cancer patients show promising results in both oncological and functional outcomes, but more information on its clinical performance is required before clinicians can integrate IRE into routine clinical practice. This narrative review describes the IRE procedure, summarises the available data about irreversible electroporation as a focal therapy for prostate cancer, and discusses future perspectives in this field.

### 3. Future Directions

So far, early studies have shown that IRE is a safe procedure that can offer good short-term oncological outcomes whilst carrying a lower risk of poor functional outcomes compared to radical treatment. Based on these results, larger comparative phase three trials are warranted to further investigate the effects of IRE and to provide meaningful long-term data for these men. Ultimately, its effects on prostate cancer metastasis and survival will determine if IRE will become an option in clinical practice guidelines.

Two challenges that remain in trial design for focal therapy are the selection criteria for men that would most benefit from this treatment and the appropriate follow-up protocols for these men. Although the niche for focal therapy lies in the treatment of localised intermediate risk prostate cancer (given low risk disease can be treated with active surveillance and high risk disease has high recurrence rates, even with radical treatment), the delineation between low, intermediate and high risk prostate cancer is still grey, given the complexity of prostate cancer risk stratification. For IRE, the size of the lesion and the number of lesions within the prostate may be significant considerations when selecting patients due to its focal nature and the in-field and out of field recurrences reported in early studies of IRE. Higher risk histological features may also contribute to these recurrences. Furthermore, the efficacy of IRE for radio-recurrent prostate cancer needs to be established. Answers to these questions require more data, which will be facilitated by the development of registry databases such as The Clinical Research Office of the Endourological Society (CROES [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02255890) identifier: NCT02255890) and Australasian IRE databases [9].

Another area of research that may impact the selection criteria and follow-up for men undergoing focal therapy treatment is the accurate identification of prostate cancer lesions. The accuracy of prostate MRI for the detection of cancer post-IRE still needs to be investigated. The addition of prostate specific membrane antigen positron emission tomography (PSMA PET) imaging may also improve the localisation of prostate cancer lesions and therefore help to characterise the prostate more accurately. Already proven in the staging of prostate cancer [9] and included in guidelines for biochemical recurrence [2], PSMA PET is now being investigated at the stage of initial diagnosis [10]. For IRE, PSMA PET has the potential to be used at the diagnosis stage to identify lesions missed by MRI, thereby helping to plan IRE probe placement. Furthermore, PSMA PET could be utilised in the follow-up of men post-IRE where recurrent lesions seen on PSMA PET imaging can be targeted by prostate biopsy.

To our knowledge, there is only one trial that is looking to compare IRE to radical prostatectomy ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04278261) identifier: NCT04278261). This group will recruit 438 men with localised prostate cancer (PSA < 20 ng/mL, T1a–T2c, Gleason score < 8) at a single centre in Shanghai. Their primary outcome measure will be 5-year tumour progression rate as seen by prostate biopsy, MRI and PSMA PET. Another group will look to compare focal IRE with extended (half-gland) IRE in 106 men with low to intermediate risk prostate cancer ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01835977) identifier: NCT01835977). Their primary outcome will be patient side effects and quality of life post-treatment. The results of these studies are eagerly awaited as clinicians and researchers look to improve the treatment paradigm for localised prostate cancer.

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