

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Irreversible electroporation for treating prostate cancer

The prostate is a small gland near a man's bladder. Prostate cancer is often diagnosed before symptoms develop, but it may present with problems in passing urine or difficulties with sexual function. In this procedure, needles are inserted through the skin into the tumour and electrical pulses are used to kill the cancer cells.

The National Institute for Health and Care Excellence (NICE) is examining irreversible electroporation for treating prostate cancer and will publish guidance on its safety and efficacy to the NHS. NICE's interventional procedures advisory committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The advisory committee has made draft recommendations about irreversible electroporation for treating prostate cancer.

This document summarises the procedure and sets out the draft recommendations made by the advisory committee. It has been prepared for public consultation. The advisory committee particularly welcomes:

- comments on the draft recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The advisory committee will meet again to consider the original evidence and its draft recommendations in the light of the comments received during consultation.

- The advisory committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 23 September 2016

Target date for publication of guidance: December 2016

1 Draft recommendations

- 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.

2 Indications and current treatments

- 2.1 Prostate cancer is usually diagnosed after a blood test in primary care has shown elevated prostate-specific antigen (PSA) levels. Most prostate cancers are either localised or locally advanced at diagnosis. Localised prostate cancer does not usually cause any symptoms, but some men might have some urinary problems or erectile dysfunction.
- 2.2 A [NICE guideline](#) describes recommendations for the diagnosis and management of prostate cancer. Current treatments for localised disease include active surveillance, radical prostatectomy, external beam radiotherapy and brachytherapy. Hormone therapy (androgen deprivation or anti-androgens) is usually the primary treatment for metastatic prostate cancer, but is increasingly being used for locally advanced, non-metastatic disease.

3 The procedure

- 3.1 The aim of irreversible electroporation is to destroy cancerous cells by subjecting them to a series of short electrical pulses using high-voltage direct current. This creates multiple holes in the cell membrane, irreversibly damaging the cell's homeostatic mechanisms and leading to cell death.
- 3.2 The procedure is done with the patient under general anaesthesia. A neuromuscular blocking agent is essential to prevent uncontrolled severe muscle contractions caused by the electric current. A number of electrode needles (typically 3–5) are introduced percutaneously and inserted into, and adjacent to, the tumour using image guidance. A series of very short electrical pulses is delivered over several minutes to ablate the tumour. The

electrodes may be repositioned to extend the zone of electroporation until the entire tumour and an appropriate margin have been ablated.

- 3.3 Cardiac synchronisation is used to time delivery of the electrical pulse within the refractory period of the heart cycle, minimising the risk of arrhythmia.

4 Efficacy

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a case series of 25 patients treated by irreversible electroporation for prostate cancer, the ablated zone was histologically clear of disease in all of the men who had a 7-month follow-up biopsy (84% [21/25] of patients). Overall, 76% (16/21) of men were histologically clear of significant disease and 38% (8/21) of men were histologically clear of any cancer at all. One patient had a significant finding in the field outside the adjacent zone; the lesion had not been detected preoperatively or on his 6-month MRI. Of the 5 patients with significant disease on follow-up biopsy, 3 remain on active surveillance, 1 is awaiting repeat irreversible electroporation and 1 had a radical prostatectomy.
- 4.2 In a case series of 34 patients, suspicious residual disease was seen on multiparametric MRI in 18% (6/34) of patients during follow-up. In 2 of these patients, prostate-specific antigen (PSA) levels dropped significantly from baseline, and they remain on surveillance. The other 4 patients had secondary treatment

(1 irreversible electroporation, 2 high-intensity focused ultrasound, 1 radical prostatectomy). Only 1 patient had histological verification of treatment failure by transperineal targeted biopsy. In a second case series of 25 patients, 28% (7/25) of men had a template biopsy that was positive for prostate cancer at 6-month follow-up. Primary failure was reported in 16% (4/25) of patients: 3 patients subsequently had surgery.

- 4.3 In the first case series of 25 patients there were no statistically significant changes in urinary symptom score, urinary function score, sexual function score, bowel function score, SF-12 physical component score or SF-12 mental component score at 6-month follow-up (n=18). Pad-free continence rates were 100%, 94%, 94% and 100% and leak-free continence rates were 67%, 53%, 65% and 67% at baseline, 6-week, 3-month and 6-month follow-up respectively. The proportion of men with erections sufficient for penetration were 44%, 38%, 47% and 56% at baseline, 6-week, 3-month and 6-month follow-up respectively. In the case series of 34 patients, potency was preserved in 95% (19/20) of men who were potent before treatment. All men who were continent before treatment were still continent afterwards (24/24). In the second case series of 25 patients, 77% (17/22), 81% (13/16) and 88% (15/17) of patients had normal urinary function at baseline, 6-month and 12-month follow-up respectively. Of the 17 patients with normal urinary function at baseline, 2 reported a decrease in score to below normal at 6-month and 1 at 12-month follow-up. At 12-month follow-up, 1 patient with normal erectile function at baseline reported new difficulty with potency. Use of incontinence pads was reported in 1 and 2 men at 6-month and 12-month follow-up respectively.

- 4.4 In a case series of 16 patients, statistically significant differences were seen in 1 domain in the Expanded Prostate Cancer Index Composite (EPIC) questionnaire: quality of life concerning urinary function decreased ($p=0.01$) at 1-week and 4-week follow-up. Quality of life concerning sexual function, hormonal function and bowel habits did not significantly decrease during follow-up.
- 4.5 The specialist advisers listed cancer control and cancer-related survival as the key efficacy outcomes.

5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Urinary retention was reported in 6% (2/34), 10% (3/30), 20% (5/25), 22% (6/27), and 38% (6/16) of patients in 5 case series of 34, 30, 25, 27 and 16 patients respectively.
- 5.2 Intermittent haematuria was reported in 24% (6/25) of patients in the case series of 25 patients (all resolved by 6 months). Debris or haematuria was reported in 18% (6/34) of patients in the case series of 34 patients. Haematuria was reported in 15% (4/27) of patients at 30-day follow-up in the case series of 27 patients (all resolved by 90 days). Mild haematuria was reported in 31% (5/16) of patients in the case series of 16 patients (resolved spontaneously in all patients within 1–27 days).
- 5.3 Dysuria was reported in 3% (3/103), 4% (1/27), 15% (5/34), and 20% (5/25) of patients in the case series of 103, 27, 34, and

25 patients respectively. Painful micturition during 4-week follow-up was reported in 13% (2/16) of patients in the case series of 16 patients.

- 5.4 Urinary tract infection was reported in 6% (1/16), 7% (2/27), and 15% (5/34) of patients in the case series of 16, 27, and 34 patients respectively.
- 5.5 Postoperative infection (cystitis, epididymo-orchitis, or other infection) was reported in 3% (3/103) of patients in a case series of 103 patients. Urosepsis was reported in 1 patient in the case series of 16 patients. The patient was admitted to hospital for 6 days and treated with intravenous antibiotics.
- 5.6 Epididymitis was reported in 7% (2/27) of patients in the case series of 27 patients. In 1 of the patients, epididymitis led to abscess formation, which was treated by simple orchiectomy. Epididymitis (grade 3) was reported in 1 patient in the case series of 30 patients.
- 5.7 Urgency and frequency (Common Terminology Criteria for Adverse Events [CTCAE] grade 2) were each reported in 13% (2/16) of patients in the case series of 16 patients. Transient urgency was reported in 4% (4/103) of patients in the case series of 103 patients. Transient incontinence was reported in 12% (12/103) of patients in the case series of 103 patients.
- 5.8 Dysejaculation was reported in 5% (5/103) of patients in the case series of 103 patients.
- 5.9 Urethral stricture (grade 3) was reported in 1 patient in the case series of 30 patients.

- 5.10 Recto-urethral fistula was reported in 1 patient in the case series of 103 patients.
- 5.11 A temporary reduction in potency (<9 months) was reported in 10% (10/103) of patients and complete reduction in potency (>3 years) in 2% (2/103) of patients in a case series of 103 patients.
- 5.12 Self-resolving tachycardia during the procedure was reported in 1 patient in the case series of 34 patients.
- 5.13 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers did not report any anecdotal adverse events. They considered that the following were theoretical adverse events: damage to the urethra, bladder, urethral sphincter and rectum.

6 Committee comments

- 6.1 The Committee noted that this procedure uses new technology, which has also been used to treat cancer in organs other than the prostate.

7 Further information

- 7.1 For related NICE guidance, see the [NICE website](#).

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IPCD: irreversible electroporation for treating prostate cancer