NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of irreversible electroporation for treating renal cancer

Treating renal cancer using pulses of electricity

Renal cancer is cancer of the kidney. Irreversible electroporation is a process that uses electrical pulses to kill cancer cells. It is applied directly to the tumour through special needles. The main difference between this procedure and some other techniques for destroying tumours is that it does not produce extreme heat or cold. This means that it may cause less damage to healthy surrounding tissues than some other procedures.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2012.

Procedure name

- Irreversible electroporation for the treatment of renal cancer

Specialist societies

- British Society of Interventional Radiology
- British Association of Urological Surgeons
- British Society of Surgical Oncology
- Faculty of Clinical Oncology at the Royal College of Radiologists.

Description

Indications and current treatment

The most common type of renal cancer in adults is renal cell carcinoma. Symptoms and signs may include pain and haematuria. Some patients are diagnosed on imaging studies during investigation for other disorders. Patients with certain genetic syndromes that predispose them to kidney tumours may be diagnosed during routine imaging surveillance. Establishing the diagnosis and assessing the prognosis of some renal tumours may be difficult and not all are actively treated.

Treatment options include laparoscopic (or open) partial or total nephrectomy, and ablation techniques including radiofrequency ablation and cryoablation. Drug therapy is commonly used for advanced renal cancer.

The aim of irreversible electroporation (IRE) 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 homeostasis mechanisms and leading to cell death. IRE is a non-thermal cell-destruction technique which may allow targeted destruction of cancerous cells with less damage to surrounding structures (such as major blood vessels), compared with other types of treatment.

What the procedure involves

The procedure is performed with the patient under general anaesthesia. A neuromuscular blocking agent is essential to prevent uncontrolled severe muscle contractions caused by the electric current. Bipolar or unipolar electrode needles are introduced percutaneously (or by open surgical or laparoscopic approaches) and guided into place in and adjacent to the tumour using imaging guidance (either computed tomography [CT] or, less commonly, ultrasound). The distance between the electrodes is confirmed by imaging to ensure that the electrodes are correctly placed parallel to one another and that sufficient current flow would be generated to ensure IRE.

Each ablation cycle consists of pulses of high-voltage direct current delivered in groups (of about 10) with a brief time for recharging between groups (a cycle is usually completed in less than 2 minutes). Electrodes may be repositioned under imaging guidance to extend the zone of electroporation until the entire tumour and an appropriate margin have been ablated. The number of ablations is determined by the volume of the target tumour. When the ablation procedure is completed, further imaging may be carried out to confirm satisfactory ablation. The total procedure time has been reported to range from 2.5 to 4.5 hours.

Cardiac synchronisation is used to time delivery of the electrical pulse within the refractory period of the heart cycle, with the aim of minimising the risk of arrhythmia. Precautions should be taken for patients with implanted electrical

devices. Ablation of lesions in the vicinity of implanted electronic devices or implanted devices with metal parts should be avoided. It is important to ensure that interventions (such as a defibrillator) and people trained to treat cardiac arrhythmias are available.

Outcome measures

The 'Response evaluation criteria in solid tumors' (RECIST) are used for measuring tumour response using X-ray, CT and magnetic resonance imaging (MRI). There are 4 categories:

- Complete response: disappearance of all target lesions.
- Partial response: 30% decrease in the sum of the longest diameter of target lesions.
- Progressive disease: 20% increase in the sum of the longest diameter of target lesions.
- Stable disease: small changes that do not meet the above criteria.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to irreversible electroporation for the treatment of renal cancer. Searches were conducted of the following databases, covering the period from their commencement to 10 July 2012: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with renal cancer.
Intervention/test	Irreversible electroporation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 21 patients with renal cancer from 3 case series[1–3].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on irreversible electroporation for the treatment of renal cancer

Abbreviations used: CT, computed tomography; ECG, electrocardiography; IRE, irreversible electroporation; RCC, renal cell carcinoma; RECIST, response evaluation criteria in solid tumors.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Thomson KR (2011)[1]

Case series
Australia
Recruitment period: 2008–9
Study population: Patients with 1 or more tumours of the target organs (liver, lung and kidney).
n=38 patients; 69 separate tumours
Age: not reported
Sex: not reported

Patient selection criteria:
Indications: Patients with 1 or more tumours of the target organs (liver, lung and kidney) in which conventional therapy was not possible or had been unsuccessful.
Contraindications include cardiac failure, recent liver embolisation and imminent liver failure from tumour load.

Technique: Nanoknife device was used (AngioDynamics, USA). IRE was performed with the patients under general anaesthesia with muscle paralysis. Adequate cardiac synchronisation was achieved with AccuSync model 72. This was used after cardiac arrhythmias were reported in 4 patients who were treated with AccuSync model 42 R-</td>
<td>Number of patients analysed: 7 patients with renal cancer (10 tumours)

Response rate (renal cancer)
<table>
<tr><th></th><th>Proportion of tumours</th></tr>
<tr><td>Complete response</td><td>50.0% (5/10)</td></tr>
<tr><td>Progressive disease</td><td>50.0% (5/10)</td></tr>
</table>
Assessed by modified RECIST at 3 months.

CT follow-up at 3 months confirmed ablation of the tumour in 5 of the 7 patients, although 2 patients needed a second IRE procedure.

Biopsy in 1 patient showed coagulative necrosis at the IRE treatment site, with patent blood vessels.</td>
<td>Key safety findings potentially related to use of IRE for renal cancer (n=7 patients, 10 procedures)
<table>
<tr><th></th><th>No. reported</th></tr>
<tr><td>Partial ureteric obstruction and increasing creatinine level (ureter previously damaged by radiofrequency ablation; treated by stent placement)[a]</td><td>14.3% (1/7)</td></tr>
<tr><td>Transient haematuria (resolved spontaneously)</td><td>28.6% (2/7)</td></tr>
<tr><td>Transient hypertension (unplanned insertion of electrode into adrenal gland; the patient subsequently had severe postural hypotension for 2 months)</td><td>14.3% (1/7)</td></tr>
</table>
[a] No evidence of stricture was seen in the other 6 patients even though the ureter or collecting system was within the treatment zone.

Key safety findings related to use of IRE (including some patients with liver cancer)
<table>
<tr><th></th><th>Number reported</th></tr>
<tr><td>Mortality at 30 days</td><td>0% (0/38)</td></tr>
<tr><td>Transient ventricular tachycardia (with inadequate ECG synchronisation)[a, b]</td><td>4 patients (no treatment needed)</td></tr>
<tr><td>Transient supraventricular tachycardia (with adequate ECG synchronisation)</td><td>1 patient (resolved without treatment)</td></tr>
<tr><td>Atrial fibrillation (with adequate ECG synchronisation)[b]</td><td>1 patient (needed cardioversion)</td></tr>
</table>
[a] In 2 procedures cardiac arrhythmia led to procedures being aborted before the planned number of ablations was</td>
<td>It is likely some reporting has been duplicated because the study centre and some of the authors are the same for references 1 and 2.

Follow-up issues:
• One patient with advanced lung cancer was lost to follow-up.

Study design issues:
• This study was designed to report outcomes in the first treatment of humans with IRE.
• No formal statistical tests were performed for data on outcome (whether there was complete response, progressive disease or stable disease).

Study population issues:
• Study recruited and reported patients with different tumours. Consequently, some of the safety findings highlighted may not relate to patients with renal cancer.</td>
</tr>
</table>

Abbreviations used: CT, computed tomography; ECG, electrocardiography; IRE, irreversible electroporation; RCC, renal cell carcinoma; RECIST, response evaluation criteria in solid tumors.

Study details	Key efficacy findings	Key safety findings	Comments
wave trigger device. Follow-up: **3 months** Conflict of interest/source of funding: One author or his department received funding/sponsorship from AngioDynamics (Queensbury, New York). None of the other authors have identified a conflict of interest.		completed (blood pressure dropped but all symptoms resolved on stopping treatment). In addition, 1 of these 4 patients developed bigeminy after resolution of ventricular tachycardia, which resolved within 24 hours without treatment. Percentages not calculated because the actual number of patients who had IRE without adequate ECG-synchronisation was not reported. [b] Timing unclear, most likely during the procedure. **Other complications** One patient experienced a brief flushing/allergic reaction after the procedure that appeared to be related to anaesthesia.	

Abbreviations used: CT, computed tomography; ECG, electrocardiography; IRE, irreversible electroporation; RCC, renal cell carcinoma; RECIST, response evaluation criteria in solid tumors.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Ball C (2010)[2]

Case series
Australia
Recruitment period: not reported
Study population: Patients with either primary or metastatic cancer, some in more than 1 site.
n=21 patients; 28 tumours
(17 liver, 8 kidney, 3 lung)
Age: mean 59 years (range 42–81)
Sex: not reported
Patient selection criteria: not reported

Technique: Nanoknife device was used (AngioDynamics, USA). IRE was performed with the patients under general anaesthesia with muscle paralysis. All patients had intra-arterial blood pressure monitoring to detect arrhythmias. An ECG synchronisation device (AccuSync Model 72) was acquired early in the study with variable success with synchronisation.

Follow-up: 24 to 48 hours

Conflict of interest/source of funding: One author received funding/sponsorship from the device manufacturer and a family member has a personal pecuniary interest. None of the other authors have identified a conflict of interest.</td>
<td>No efficacy data were reported in the paper.</td>
<td>Key safety findings potentially related to use of IRE for renal cancer
<table>
<tr><th></th><th>Procedures % [n/N]</th></tr>
<tr><td>Ventricular bigeminy on induction of anaesthesia and intermittently throughout IRE procedure</td><td>3.6 (1/28)</td></tr>
<tr><td>Brief runs of ventricular tachycardia (arterial blood pressure was markedly decreased in 4 of the 7 procedures)</td><td>25.0 (7/28) (including 1 patient with renal tumours)</td></tr>
<tr><td>Extreme increases in blood pressure (up to 200/100 mmHg from a baseline of 140/60 mmHg)[a]</td><td>7.1 (2/28) (both patients had renal tumours)</td></tr>
<tr><td>Transient increase in systolic blood pressure of approximately 20 to 30 mmHg after the treatment cycles[b]</td><td>100 (all patients)</td></tr>
<tr><td>Postoperative pain</td><td>46.4 (13/28)</td></tr>
<tr><td>Acid-base disturbances with associated hyperkalaemia[c]</td><td>14.3 (4/28)</td></tr>
</table>
[a] In 1 patient, the increase was sustained beyond a few minutes and medical treatment was given; the electrodes were subsequently checked and thought to be in the adrenal gland. There were no problems with further treatment cycles after the electrodes were repositioned.
[b] This increase was not modified by opioids, was not sustained beyond a few minutes, and did not need treatment.
[c] None of these patients had disturbances that were significant enough to limit the duration of the procedure; 3 patients had pre-existing renal impairment.
Other complications
In inadequately paralysed patients, the discharge of the electrodes produced contractions of the entire upper body with each pulse, similar to that seen with a grand mal seizure (actual numbers not reported). When patients were adequately paralysed, some muscular contractions were</td>
<td>It is likely some reporting has been duplicated because the study centre and some of the authors are the same for references 1 and 2.

Follow-up issues:
• Patients were only followed up for 24 to 48 hours.

Study design issues:
• The CT scanning room was not initially designed for procedures needing anaesthesia and presented challenges of remote anaesthesia practice.
• Formal method to assess postoperative pain not reported.
• Study only reported safety findings but no reports on efficacy of IRE.

Study population issues:
• Study recruited and reported patients with different tumours, not specific to renal cancer. Consequently, some of the safety findings highlighted may not relate to patients with renal cancer.</td>
</tr>
</table>

Abbreviations used: CT, computed tomography; ECG, electrocardiography; IRE, irreversible electroporation; RCC, renal cell carcinoma; RECIST, response evaluation criteria in solid tumors.

Study details	Key efficacy findings	Key safety findings	Comments
		still visible, mainly confined to the treatment area but sometimes including the diaphragm. These contractions are probably caused by direct muscle stimulation.	

Abbreviations used: CT, computed tomography; ECG, electrocardiography; IRE, irreversible electroporation; RCC, renal cell carcinoma; RECIST, response evaluation criteria in solid tumors.

Study details	Key efficacy findings	Key safety findings	Comments
Pech M (2011)[3] **Case series** Germany Recruitment period: not reported Study population: patients scheduled for surgical resection of RCC **n=6** Age: mean 58 years (range 44–73) Sex: 50% (3/6) male Patient selection criteria: patients scheduled for surgical resection of RCC measuring < 4 cm and without any sign of metastasis. Technique: NanoKnife IRE electroporator (AngioDynamics, New York) was used with a bipolar electrode. IRE was done immediately before surgical resection, with ECG synchronisation. The entire procedure was monitored by ultrasonography. Follow-up: **12 weeks** Conflict of interest/source of funding: none	Number of patients analysed: **6** No efficacy data were reported – the purpose of the study was to assess the feasibility and safety of ablating RCC tissue by IRE.	There was a single case of intraoperative supraventricular extrasystole (with ECG synchronisation). No ECG-related changes were seen in the postoperative monitoring phase or at follow-up (after 12 weeks). There were no changes in cardiac function after IRE.	**Study design issues**: • Small safety-only pilot study. • The authors noted that this pilot study was intentionally restricted to a small patient population and to an overall procedure that deviated as little as possible from the standard resection. • The 15-minute interval between IRE and resection was only sufficient to show any immediate histological effects.

Efficacy

Tumour response

A case series of 38 patients, of whom 7 had renal cancer (10 tumours), reported a complete response in 50% (5/10) of tumours and progressive disease in 50% (5/10) of tumours at 3-month follow-up (assessed by modified RECIST)[1]. Two of the 5 patients with a complete response were treated by a second IRE procedure[1]. In the same series, a biopsy in 1 patient with renal cancer showed coagulative necrosis at the IRE treatment site, with patent blood vessels.

Safety

Cardiac arrhythmia

Transient ventricular arrhythmia was reported in 4 patients with inadequate synchronisation in the case series of 38 patients (timing unclear, most likely during the procedure)[1]. No cardioversion or other treatment was needed. One of the 4 patients developed bigeminy after ventricular tachycardia resolved. The bigeminy resolved within 24 hours without treatment. One patient with adequate cardiac synchronisation reported transient supraventricular tachycardia, which resolved without treatment. One patient who had adequate cardiac synchronisation developed atrial fibrillation and needed cardioversion after the IRE procedure.

Transient ventricular tachycardia was reported during 25% (7/28) of procedures in a case series of 21 patients with primary or metastatic cancer (liver, kidney and lung)[2]. Arterial blood pressure was 'markedly decreased' in 4 of the 7 procedures. The authors noted that a synchronisation device was used from early in the trial, but they had variable success with synchronisation.

Intraoperative supraventricular extrasystole was reported in 1 patient in a case series of 6 patients. No electrocardiography (ECG)-related changes were detected after the procedure or at follow-up (after 12 weeks)[3].

Ureteric obstruction

Partial ureteric obstruction and increasing creatinine level were reported in 1 patient with renal cancer in the case series of 38 patients (timing not reported). The patient's ureter had been damaged previously by radiofrequency ablation. The obstruction was treated by inserting a ureteric stent[1].

Hypertension

Extreme increases in blood pressure during the procedure (up to 200/100 mmHg from a baseline of 140/60 mmHg) were reported in 7% (2/28) of procedures in the case series of 21 patients with tumours in the liver, kidney or lung (both

patients were treated for renal cancer)[2]. In 1 patient, the blood pressure increase lasted for more than a few minutes and medical treatment was needed. The position of the electrodes was subsequently checked and thought to be in the adrenal gland. Transient increases in systolic blood pressure of approximately 20 to 30 mmHg after treatment cycles were reported for all patients in the same study[2].

Muscle spasms

Contractions of the entire upper body, similar to that seen with a grand mal seizure, with each pulse of the electrodes was reported in patients who were inadequately paralysed (absolute numbers not reported) in the case series of 21 patients with primary or metastatic liver, kidney or lung cancer[2]. When patients were adequately paralysed, some muscular contractions were still visible, mainly confined to the treatment area but sometimes including the diaphragm. The authors noted that these contractions were probably caused by direct muscle stimulation.

Validity and generalisability of the studies

- The evidence consists of 3 small case series, including approximately 21 patients with renal cancer.
- Only 1 study reported efficacy data[1]. The remaining 2 studies focused on safety outcomes.
- Two studies included patients with liver, lung or kidney tumours[1,2]; some outcomes were not reported separately by indication so it was difficult to identify safety findings specifically for renal cancer.
- There are no long-term or comparative data.
- There is likely to be some patient overlap between the studies.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Single-port laparoscopic nephrectomy. NICE interventional procedures guidance 414 (2011). Available from www.nice.org.uk/guidance/IPG414
- Laparoscopic cryotherapy for renal cancer. NICE interventional procedures guidance 405 (2011). Available from www.nice.org.uk/guidance/IPG405

- Percutaneous cryotherapy for renal cancer. NICE interventional procedures guidance 402 (2011). Available from www.nice.org.uk/guidance/IPG402
- Percutaneous radiofrequency ablation for renal cancer. NICE interventional procedures guidance 353 (2010). Available from www.nice.org.uk/guidance/IPG353
- Laparoscopic partial nephrectomy. NICE interventional procedures guidance 151 (2006). Available from www.nice.org.uk/guidance/IPG151
- Laparoscopic nephrectomy (including nephroureterectomy). NICE interventional procedures guidance 136 (2005). Available from www.nice.org.uk/guidance/IPG136

Technology appraisals

- Pazopanib for the first-line treatment of advanced renal cell carcinoma. NICE technology appraisal 215 (2011). Available from www.nice.org.uk/guidance/TA215
- Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma. NICE technology appraisal 169 (2009). Available from www.nice.org.uk/guidance/TA169

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr M Aitchison (British Association of Urological Surgeons), Professor E Leen (Royal College of Radiologists).

- One Specialist Adviser has performed the procedure at least once and one has never performed the procedure.
- One Specialist Adviser considers the procedure to be a minor variation on an existing procedure, the other considers it to be definitely novel and of uncertain safety and efficacy.
- Comparators to the procedure are cryoablation and radiofrequency ablation.
- Theoretical adverse effects include damage to surrounding organs, ventricular tachycardia/atrial fibrillation, minor bleeding, sepsis and ureteric stricture.
- Key efficacy outcomes include local tumour control, time to progression, and overall survival.
- There are uncertainties or concerns about the long-term efficacy of the procedure.

- Patient selection should be done by a uro-oncology multidisciplinary team.
- Interventional radiological training, imaging and anaesthetic support are needed.
- Both Specialist Advisers consider the potential impact on the NHS to be minor.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

None other than those described above.

References

1. Thomson KR, Cheung W, Ellis SJ et al. (2011) Investigation of the safety of irreversible electroporation in humans. Journal of Vascular and Interventional Radiology 22: 611–21

2. Ball C, Thomson KR, Kavnoudias H (2010) Irreversible electroporation: a new challenge in ‘out of operating theater’ anesthesia. Anesthesia & Analgesia 110: 1305–9

3. Pech M, Janitzky A, Wendler JJ et al. (2011) Irreversible electroporation of renal cell carcinoma: a first-in-man phase I clinical study. Cardiovascular and Interventional Radiology 34: 132–8

Appendix A: Additional papers on irreversible electroporation for the treatment of renal cancer

There were no additional papers identified.

Appendix B: Related NICE guidance for irreversible electroporation for the treatment of renal cancer

Guidance	Recommendations
Interventional procedures	**Single-port laparoscopic nephrectomy. NICE interventional procedures guidance 414 (2011).** 1.1 Evidence on the safety and efficacy of single-port laparoscopic nephrectomy is based on limited numbers of patients. Any advantage for patients of the procedure over conventional laparoscopic nephrectomy is uncertain and there is inadequate evidence on safety, including insufficient information about warm ischaemia time when used to harvest kidneys from live donors for transplantation. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake single-port laparoscopic nephrectomy should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for patients (Understanding NICE guidance) is recommended. • Audit and review clinical outcomes of all patients having single-port laparoscopic nephrectomy (see section 3.1). 1.3 Patient selection is particularly important when the procedure is being considered for the treatment of patients with malignant disease. 1.4 Single-port laparoscopic nephrectomy is technically challenging and should only be carried out by experienced laparoscopic surgeons who have received specific training in the procedure. 1.5 NICE encourages the publication of further evidence on single-port laparoscopic nephrectomy. In particular, clinicians are encouraged to collect and publish data on long-term recurrence rates when the procedure is used to treat malignancy and on subsequent graft survival and renal function when it is used for donor nephrectomy. NICE may review the procedure on publication of further evidence.

	Laparoscopic cryotherapy for renal cancer. NICE interventional procedures guidance 405 (2011). 1.1 Current evidence on the efficacy and safety of laparoscopic cryotherapy for renal cancer is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 This procedure should only be offered after assessment by a specialist urological cancer multidisciplinary team. 1.3 NICE encourages collection and publication of data on the long-term outcomes of this procedure. **Percutaneous cryotherapy for renal cancer. NICE interventional procedures guidance 402 (2011).** 1.1 Current evidence on the efficacy and safety of percutaneous cryotherapy for renal cancer is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 This procedure should only be offered after assessment by a specialist urological cancer multidisciplinary team. 1.3 NICE encourages collection and publication of data on the outcomes of this procedure in the long term. Further research should compare the long-term outcomes of cryotherapy with those of other treatments for renal cancer. **Percutaneous radiofrequency ablation for renal cancer. NICE interventional procedures guidance 353 (2010).** 1.1 Current evidence on the safety and efficacy of percutaneous radiofrequency ablation (RFA) for renal cancer in the short and medium term appears adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit, and provided that patients are followed up in the long term. 1.2 Patient selection for percutaneous RFA for renal cancer should be carried out by a urological cancer multidisciplinary team. 1.3 NICE encourages data collection to provide information about the outcomes of this procedure in the long term. Further research should compare the long-term outcomes of RFA with those of other treatments for renal cancer.

	Laparoscopic partial nephrectomy. NICE interventional procedures guidance 151 (2006). 1.1 Current evidence on laparoscopic partial nephrectomy suggests that it is safe and efficacious when undertaken by surgeons with special expertise in this technique. Surgeons undertaking laparoscopic partial nephrectomy should have specific training and regular experience in laparoscopic renal surgery. 1.2 Clinicians wishing to undertake this procedure should ensure that patients fully understand the risks, including that of serious haemorrhage. In addition, use of the Institute's information for the public is recommended. 1.3 Clinicians should audit and review their results. The British Association of Urological Surgeons runs a cancer registry, and clinicians are encouraged to enter all patients undergoing laparoscopic partial nephrectomy onto this database. **Laparoscopic nephrectomy (including nephroureterectomy). NICE interventional procedures guidance 136 (2005).** 1.1 Current evidence on the safety and efficacy of laparoscopic nephrectomy (including nephroureterectomy) appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection is important when this procedure is being considered for the treatment of malignant disease. Long-term follow-up data are lacking, and clinicians are encouraged to collect data on rates of recurrence in patients with malignant disease.

Technology appraisals	**Pazopanib for the first-line treatment of advanced renal cell carcinoma. NICE technology appraisal 215 (2011).** 1.1 Pazopanib is recommended as a first-line treatment option for people with advanced renal cell carcinoma • who have not received prior cytokine therapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 **and** • if the manufacturer provides pazopanib with a 12.5% discount on the list price, and provides a possible future rebate linked to the outcome of the head-to-head COMPARZ trial, as agreed under the terms of the patient access scheme and to be confirmed when the COMPARZ trial data are made available. 1.2 When using ECOG performance status, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect ECOG performance status and make any adjustments they consider appropriate. 1.3 People who are currently being treated with pazopanib for advanced metastatic renal cell carcinoma but who do not meet the criteria in 1.1 should have the option to continue their therapy until they and their clinicians consider it appropriate to stop. **Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma. NICE technology appraisal 169 (2009).** 1.1 Sunitinib is recommended as a first-line treatment option for people with advanced and/or metastatic renal cell carcinoma who are suitable for immunotherapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. 1.2 When using ECOG performance status score, clinicians should be mindful of the need to secure equality of access to treatments for people with disabilities. Clinicians should bear in mind that people with disabilities may have difficulties with activities of daily living that are unrelated to the prognosis of renal cell carcinoma. In such cases clinicians should make appropriate judgements of performance status taking these considerations into account. 1.3 People who are currently being treated with sunitinib for advanced and/or metastatic renal cell carcinoma but who do not meet the criteria in 1.1 should have the option to continue their therapy until they and their clinicians consider it appropriate to stop.

Appendix C: Literature search for irreversible electroporation for the treatment of renal cancer

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	13/07/2012	July, 2012	27
Database of Abstracts of Reviews of Effects – DARE (CRD website)	13/07/2012	July, 2012	6
HTA database (CRD website)	13/07/2012	July, 2012	26
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	13/07/2012	July, 2012	57
MEDLINE (Ovid)	13/07/2012	1946 to July Week 1 2012	677
MEDLINE In-Process (Ovid)	13/07/2012	July 12, 2012	22
EMBASE (Ovid)	13/07/2012	1974 to 2012 week 27	1640
CINAHL (NLH Search 2.0 or EBSCOhost)	13/07/2012	N/A	190
BLIC (Dialog DataStar)	13/07/2012	N/A	0

Trial sources searched on 10 July 2012

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Electroporation/
2	Electric Stimulation/
3	exp Nanotechnology/
4	nanoknife.tw.
5	(irrevers* adj3 (electropor* or electro-por* or electropermeab* or electro-permeab*)).tw.
6	(electric* adj3 (field* or stimul* or pulse* or cell? or membrane* or pore?)).tw.
7	Electric Stimulation Therapy/
8	IRE.tw.
9	LEDC.tw.
10	Electrochemotherapy/
11	electrochemo*.tw.
12	Ablation Techniques/
13	((tissue* or tumor* or tumour*) adj3 ablat*).tw.
14	(bipolar adj3 (puls? or electrod* or mode?)).tw.
15	or/1-14
16	Prostatic Neoplasms/
17	(Prostat* adj3 (Neoplasm* or Cancer* or Carcinoma* or Adenocarcinom* or Tumour* or Tumor* or Malignan* or Lump* or Masses*or Sarcoma* or Metastasis*)).tw.
18	16 or 17
19	Carcinoma, Renal Cell/
20	exp Kidney Neoplasms/
21	((kidney* or renal* or Grawitz* or Transitional* or Wilm* or Nephroid or hypernephroid or hypernephroma*) adj3 (Neoplasm* or Cancer* or Carcinoma* or Adenocarcinom* or Tumour* or Tumor* or Malignan* or Lump* or Masses* or Sarcoma* or Metastasis*)).tw.
22	(Nephroblastoma* or nephroma*).tw.

23	or/19-22
24	15 and 18
25	15 and 23
26	24 or 25
27	animal/ not human/
28	**26 not 27**