NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: tristan.mckenna@nice.org.uk

Procedure Name:	IP1023/2 Irreversible electroporation for treating pancreatic cancer
Name of Specialist Advisor:	Dr Breen
Specialist Society:	**British Society of Gastrointestinal and Abdominal Radiology (BSGAR)**

1 Do you have adequate knowledge of this procedure to provide advice?

x☐ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

x☐ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

x☐ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

x☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

I have wide experience in image-guided ablation and have done these particular procedures- specifically IRE for locally advanced Pancreatic cancer- under proctoring in institutions abroad.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

x☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

At present we refer away for IRE in LAPC, on occasion.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

x☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I have wide clinical and research experience in image-guided ablation but to a lesser extent with IRE in particular. I am however entirely familiar with this arena.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

x☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Some 3 years ago, at last NICE review, this was definitely novel. Accrued experience has no down-graded this to a more standard procedure, but in the case of LAPC still one needing careful audit.

3.2 What would be the comparator (standard practice) to this procedure?

Resection, rather than other ablative procedures, which have not been borne out for LAPC.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

X☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

Very few and I feel this should be confined to centres with considerable experience in IGA(image-guided ablation), so as to ensure safe practice.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

These largely amount to pancreatitis(~12%) and benign abdominal pain. Almost nil gut perforation or bleeding.

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Still safety and overall survival and 2 years and towards 5 yr OS. Local tumour progression remains a difficult read-out in this setting/ in the region of an IRE ablation zone.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

It is still early days in terms of 2 and 5yr OS but I believe that safety has now been established –in skilled centres with careful case selection- since NICE reviewed this topic 3 years ago.

4.4 What training and facilities are needed to do this procedure safely?

Abundant IGA(image-guided ablation) experience under GA, with appropriate proctoring for early cases.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

A UK-wide Registry is just opening under the lead of Prof Derek Manas at Freeman, Newcastle.
Please see Narayanan G- ASCO Abstract 2014 concerning LAPC and stage 4 patients. Same author has article in print with JVIR, due for publication in October issue(50 LAPC patients).
Also Martin RC(200 patients) Ann Surg. 2015 Sep;262(3):486-94; discussion 492-4.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

Please see Narayanan paper upcoming in October edition of JVIR? And 2014 ASCO GI abstract.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

As above- needs skilled IGA centres and I believe diligent CTguided or intraoperative technique.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Safety
2yr and 5yr OS at time from diagnosis as patients at present have often already failed multiple lines of therapy.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

as above.

5.2 Adverse outcomes (including potential early and late complications):

as above.

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

slowly.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

x☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

x☐ Minor.

Comments:
This technique will be confined to limited numbers of LAPC patients.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

as above.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☐ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 **Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee**

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x ☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	x ☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	x ☐	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	x ☐	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	x ☐	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	x ☐	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	x ☐	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	x ☐	**NO**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair	**Professor Carole Longson, Director, Centre for Health Technology Evaluation.**

Jan 2016

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

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Interventional Procedures Programme

Specialist Adviser questionnaire

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Please respond in the boxes provided.

Please complete and return to: tristan.mckenna@nice.org.uk

Procedure Name:	IP1023/2 Irreversible electroporation for treating pancreatic cancer
Name of Specialist Advisor:	Dr Peter Littler
Specialist Society:	**British Society of Interventional Radiology (BSIR)**

1 Do you have adequate knowledge of this procedure to provide advice?

X Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

X Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X Yes.

No Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

X I do this procedure regularly.

Comments:

I have done 8 pancreatic IRE cases (2 open). The UK registry contains 21 cases from three centres (6 of these open). A significant number (over 30) have been carried out in the private sector by a single operator. These are due to be added to the registry in the near future.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

X I take part in patient selection or refer patients for this procedure regularly.

Comments:

Cases are reviewed at our tertiary HPB MDT. I always assess the cases for suitability and ask for external opinion when necessary.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

X I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I am a co-author on a systematic review

Eur J Surg Oncol. 2014 Dec;40(12):1598-604. doi: 10.1016/j.ejso.2014.08.480. Epub 2014 Sep 28.
Systematic review of irreversible electroporation in the treatment of advanced pancreatic cancer.
Moir J1, White SA2, French JJ2, Littler P2, Manas DM2.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

X Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

There is a mounting body of evidence worldwide for safety and efficacy, however a prospective RCT is needed.

In the UK, a clinician interest group has collaborated with pancreatic cancer UK who have agreed to fund a UK wide registry. A UK multicentre trial (UNIPAC) is planned comparing IRE plus chemo vs chemo in patients with locally advanced pancreatic cancer.

3.2 What would be the comparator (standard practice) to this procedure?

Chemotherapy- Folfirinox (ACCORD 11 Trial, Conroy et al, NEJM 2011) also Gemcitabine and Gemcitabine + NabPaclitaxel depending on fitness levels etc.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

X Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

There are currently 5 Consultant Radiologists doing this procedure in the UK, Four in NHS hospitals and one in a private hospital.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

37% complication rate (median grade 2 (range 1-5)) in a prospective registry of 200 patients in predominantly open IRE.

Ann Surg. 2015 Sep;262(3):486-94;

Treatment of 200 locally advanced (stage III) pancreatic adenocarcinoma patients with irreversible electroporation: safety and efficacy.

Martin RC, Kwon D, Chalikonda S, Sellers M, Kotz E, Scoggins C, McMasters KM, Watkins K.

44% complication rate (11 of 24 (3 serious) in percutaneous IRE

Eur J Surg Oncol. 2016 Feb 10. pii: S0748-7983(16)00094-9. doi: 10.1016/j.ejso.2016.01.024. [Epub ahead of print]

Percutaneous irreversible electroporation for treatment of locally advanced pancreatic cancer following chemotherapy or radiochemotherapy.

Månsson C1, Brahmstaedt R2, Nilsson A2, Nygren P3, Karlson BM2.

Mortality ranges from 0% to 17%* (in the primary treated group - 5 of 29 - single centre experience)

*** Ann Surg Oncol. 2016 May;23(5):1736-43. doi: 10.1245/s10434-015-5034-x. Epub 2015 Dec 29.**

Single-Institution Experience with Irreversible Electroporation for T4 Pancreatic Cancer: First 50 Patients.

Kluger MD1, Epelboym I2, Schrope BA2, Mahendraraj K2, Hecht EM3, Susman J4, Weintraub JL4, Chabot JA2.

0% in mortality of 24 patients percutaneously treated

Eur J Surg Oncol. 2016 Feb 10. pii: S0748-7983(16)00094-9. doi: 10.1016/j.ejso.2016.01.024. [Epub ahead of print]

Percutaneous irreversible electroporation for treatment of locally advanced pancreatic cancer following chemotherapy or radiochemotherapy.

Månsson C1, Brahmstaedt R2, Nilsson A2, Nygren P3, Karlson BM2.

2. Anecdotal adverse events (known from experience)

Pancreatic leak from treated NET tumour, haematoma, vessel occlusion (transient due to oedema post IRE causing compression of an involved SMV or permanent), Marked pain for several hours post procedure requiring opiod analgesia.

3. Theoretical adverse events

Bleeding, infection, bile leak, vessel thrombosis/ occlusion, pancreatic leak, bowel perforation, pancreatitis.

4.2 What are the key efficacy outcomes for this procedure?

Progression free survival, Overall survival.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

There are uncertainties regarding the efficacy of the procedure due to the relative paucity of evidence, particularly in the percutaneous setting.

It is the percutaneous approach that is most likely to be used in Europe/ UK , with the advantage of not subjecting patients with incurable cancer and limited life expectancy to an open operation.

4.4 What training and facilities are needed to do this procedure safely?

The operator should have extensive background of experience in thermal tumour ablations, have a reasonable experience of using IRE in the liver and/or kidney and undergo mentorship/ proctoring of IRE pancreas cases.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

UK pancreatic IRE registry – supported by Pancreatic Cancer UK
ERI PAC trial (UK, multicentre) planned but not yet recruiting.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

No. Please note the patient information pages on the Pancreatic Cancer UK website.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

There is uncertainty regarding the best approach (percutaneous or open). Most of the published evidence is for open (Martin, USA) but European practice favours percutaneous.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Lesion size, location, presence of a metal stent, procedural details (number of pulses, number of needles, electrode exposure and repositionings), Adverse events, follow up imaging at a minimum of 3 monthly intervals, Progression Free Survival , Overall Survival, other treatments (chemo/ radiotherapy).

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

Pain scores/ Quality of Life.

5.2 Adverse outcomes (including potential early and late complications):

See above.

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

I think use of this procedure will spread slowly until there is high quality evidence. Once available, the numbers will increase assuming positive outcomes.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

X Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

It is technically demanding procedure and is likely to be carried out by a few operators in the UK in Tertiary centres.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

X Minor.

Comments:
Whilst there will be an increase in numbers of pancreatic IRE treatments over the coming years, I think that the numbers treated ultimately per year in the UK will not be large (below 100).

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

None in addition to the planned literature search.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

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☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 **Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee**

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

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Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	X	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	**X**	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	X	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	X	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	X	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	X	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	X	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	X	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:
I have acted as a proctor for Angiodynamics once in 2015 to support a new centre starting to use IRE technology (for a renal IRE in Leeds Hospital). This attracted a fee of apx £1000. I have not proctored for pancreatic IRE.

Thank you very much for your help.

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

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2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: tristan.mckenna@nice.org.uk

Procedure Name:	IP1023/2 Irreversible electroporation for treating pancreatic cancer
Name of Specialist Advisor:	Mr Dr Parthipun
Specialist Society:	**British Society of Interventional Radiology (BSIR)**

1 Do you have adequate knowledge of this procedure to provide advice?

● Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

● Yes.
☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

● Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

- **I have done this procedure at least once.**

☐ I do this procedure regularly.

Comments:

I have performed 5 IRE ablations in the last 18 months and have collected the outcome data for 31 patients performed at King's College Hospital, London

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

- **I have taken part in patient selection or referred a patient for this procedure at least once.**

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

- Other (please comment)

I have collected and presented the data from King's College Hospital at BSIR (British Society of Interventional Radiology):
"Initial results for the use of Irreversibel electroporation for the treatment of intra-abdominal malignant lesions in a single institution" – BSIR, Glasgow Nov 2015.
(This study included 10 patients who underwent IRE for pancreatic lesions but also a further 20 patients who have undergone intra-abdominal IRE)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

This is an established procedure but long term results and larger studies are still awaited

3.2 What would be the comparator (standard practice) to this procedure?

Thermal ablation (microwave ablation)

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

- Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

Very few interventional radiologists perform this procedure in the UK. < 10%

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Cardiac arrhythmias – depends on the distance from the heart. Therefore synchronization of the IRE pulses with cardiac rhythm (via ECG synchronization) is advised

Pancreatitis- Narayanan et al evaluated safety of percutaneous IRE in 15 patients. One patient developed grade 2 pancreatitis

Pancreatic abscesss - Paiella et al reported 1 out of 10 patients developed a liver abscess in their series (Overall complication 2 out of 10 patients)

Pancreaticoduodenal fistula - Paiella et al reported 1 out of 10 patients developed a liver abscess in their series (Overall complication 2 out of 10 patients)

Bile leak – Martin et al series demonstrated

Portal vein thrombosis – Martin et al series

References:

Narayana G, et al. Percutaneous irreversible electroporation for down staging and control of unresectable pancreatic adenocarcinoma. J Vasc Interv Radiol 2012; 23: 1613 -1621

Paiella et al. Safety and feasibility of irreversible electroporation (IRE) in patients with locally advanced pancreatic cancer: results of a prospective study. JDig. Surg 2015; 32: 90-97

Martin RC et al. Irreversible electroporation therapy in the management of locally advanced pancreatic adenocarcinoma. J Am Coll Surg 2012; 215:361-369

Martin RC et al. Irreversible electroporation therapy in locally advanced pancreatic cancer: potential improved overall survival. Ann Surg Oncol 2013; 20 (suppl 3): S443- S449

Martin RC et al. Treatment of 200 locally advanced (Stage III) pancreatic adenocarcinoma patients with irreversible electroporation: safety and efficacy. Ann Surg 2015; 262: 486- 494

2. Anecdotal adverse events (known from experience)

Cardiac arrhythmias. If the patient develops significant tachycardia (> 150bpm), the IRE machine has a safety cut off and will not operate

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

- **Reduction in the size of the tumour (partial response or complete response)**
- **Local tumour control**
- **Increase in relapse free patient survival**
- **Increase in overall survival**

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

There are a lack of publish data regarding IRE. The vast number of studies have been performed at single centres on low number of patients. Large multicentre, randomised studies are recommended before formal conclusions can be made.

4.4 What training and facilities are needed to do this procedure safely?

The operator must have extensive experience in thermal ablative modalities such as microwave, RFA and cryotherapy in addition to being technical fluent with the use of high quality intraoperative procedural imaging mostly involving ultrasound and CT.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

unaware

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

"Initial results for the use of Irreversibel electroporation for the treatment of intra-abdominal malignant lesions in a single institution" – BSIR, Glasgow Nov 2015. Parthipun A, Peddu P (King's College Hospital)

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

There are a lack of publish data regarding IRE. The vast number of studies have been performed at single centres on low number of patients. Large multicentre, randomised studies are recommended before formal conclusions can be made.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

Tumour free survival
Complete response
Partial response
Progressive response

5.2 Adverse outcomes (including potential early and late complications):

Immediate complications (e.g. intraprocedural atrial fibrillation), post operative pain, pancreatitis

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

If there is good evidence and large centre data, then up take would be quicker however limited by the number of people trained to do the procedure.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

● A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

● Minor.

Comments: As this will be limited by the number of interventional radiologists who have been trained in IRE

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐ **YES** • **NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐ **YES** • **NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐ **YES** • **NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐ **YES** • **NO**
Investments – any funds that include investments in the healthcare industry	☐ **YES** • **NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐ **YES** • **NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐ **YES** • **NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐ **YES** • **NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: tristan.mckenna@nice.org.uk

Procedure Name:	IP1023/2 Irreversible electroporation for treating pancreatic cancer
Name of Specialist Advisor:	Dr Chew
Specialist Society:	**British Society of Gastrointestinal and Abdominal Radiology (BSGAR)**

1 Do you have adequate knowledge of this procedure to provide advice?

X Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

X Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☐ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

X No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:
Collaborative procedure between surgeons and interventional radiologists.

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

X I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

X I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

X I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

X Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

3.2 What would be the comparator (standard practice) to this procedure?

Chemotherapy followed by surgery

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

X Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Overall complication rate was 19 % and includes A) Dysrhythmia (SVT/AF) B) Pancreatitis C) Haematoma D) Pneumothorax E)Bile leak F) Portal Vein thrombosis G) Death (post operative not periprocedural death - 2.3%) **[HJ Scheffer et al. Irreversible Electroporation for NonThermal Tumor Ablation in Clinical Setting : A Systematic Review of Safety and Efficacy. J Vasc Interv Radiol ; 2014; 25:997-1011.]**

:

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Disease free survival; Overall survival.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Yes. Uncertain benefits over standard practice.

4.4 What training and facilities are needed to do this procedure safely?

Surgeons who are capable of performing pancreatic resections and radiologists who have the technical skills and equipment to perform this procedure.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

AHPBA Pancreatic Irreversible Electroporation (IRE) Registry
Study of Combined Therapy for Pancreatic Cancer (IRE + NK cells)
Anti-tumor Immunity Induced by IRE of Unresectable Pancreatic Cancer
Outcomes of Ablation of UnresectablePancreatic Cancer Using the NanoKnife Irreversible Electroporation (IRE) System
CrossfireTrial : Comparing efficacy of IRE with Radiotherapy
PANFIRE Trial : IRE to treat locally advanced Pancreatic Cancer
IRE for Inoperable Hepatic and Pancreatic Malignancy
Effects of Dexmedetomidine during IRE procedures for Solid Tumors (Complete)
Effectivity and Safety of Irreversible Electroporation for Refractory Neoplasms in Liver and Pancreas
Study of FOLFIRINOX electrochemotherapy in the treatment of Pancreatic Adenocarcinoma
Evaluation of Safety and Efficacy of Electrochemotherapy in the treatment of Pancreatic Adenocarcinoma.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

ASCO 2016 Annual Meeting : Multimodality treatment of 132 consecutive patients with locally advanced pancreatic Cancer. J.A Vogel et al.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Lack of clinical trial evidence.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures):

Disease free survival, overall survival, symptom free survival, hospital stay, complication rate, narcotic use, qol, pain scores.

5.2 Adverse outcomes (including potential early and late complications):

Dysrhythmias, haemorrhage, pancreatitis, portal vein thrombosis, pneumothorax, death

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

Not quickly

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

X Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

X Moderate.

☐ Minor.

Comments:

Potentially if this is proven to be efficacious in locally advanced pancreatic cancer, then potentially this could largely replace surgery in this group of patients.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Outcome of several studies including 2 randomised trials are awaited.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 **Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee**

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	X	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	X	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	X	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	X	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	X	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	X	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	X	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	X	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.