NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Contact X-ray brachytherapy (Papillon) for early stage rectal cancer (1234/1)**
Name of Specialist Advisor:	**Dr Alexandra Stewart**
Specialist Society:	**Royal College of Radiologists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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?

☐ Yes.

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

Comments:

Contact X-ray brachytherapy (Papillon) for early stage low rectal cancer

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X☐ Yes.

X☐ 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 two 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 which does this procedure, please indicate your experience with it:

☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

X☐ I perform 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.

☐ 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):

X☐ I have undertaken bibliographic research on this procedure.

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

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

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

X☐ Other (please comment)

Comments:

I am involved in setting up the Opera trial whoch will offer this treatment to patients within the randomised trial setting. I am also in the early stages of setting up a registry to register non trial patients undergoing the procedure and making a national database to enter patient details into.

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 that procedure's safety and efficacy.

X☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

This procedure has an established history with efficacy but only in a few centres and is not mainstream practice yet.

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

Total mesorectal excision of the rectum either as abdomino-perineal excision or anterior resection.

3.3 Please estimate the proportion of doctors in your specialty who are performing 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:

Four hospitals in the UK-each with two specialists performing this. Several more sites interested in developing the technique.

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

2. Anecdotal adverse events (known from experience)

   Bowel perforation, bleeding, recurrence of tumour, ulceration

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

   Bowel perforation, bleeding, recurrence of tumour, ulceration

Authors Prof Sun Myint, Prof JP Gerard

4.2 What are the key efficacy outcomes for this procedure?

Local recurrence, stoma free survival, overall survival

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

This procedure carries a higher risk of local recurrence than surgery but a lower morbidity, particularly in the elderly. It appears to have the same overall survival though a phase 3 trial is awaited (opera trial). It is important that a patient undergoing the procedure is counselled appropriately about the slightly higher risk of recurrence and the need for close surveillance in the first two years to watch for local recurrence.

4.4 What training and facilities are required to undertake this procedure safely?

Must be trained at a Papillon course with hands on training at a Papillon centre.
This must be administered in an appropriately shielded room with a Papillon machine and immobilisation equipment.

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

In late phase of set up-Opera trial. In early phase of set up registry study. National database nearly ready to open

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, e.g. PUBMED? (This can include your own work). If yes, please list.

We have had two abstracts accepted for American Brachytherapy Society and ESTRO which describe our first four months experience of the procedure

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

Some surgeons believe that a patient should have a procedure with the lowest risk of recurrence no matter what the toxicity is. Others believe that a well informed patient can make a treatment choice based on their own preference if they are adequately counselled about the risk of recurrence and the need for surveillance.

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):

Local recurrence, stoma free survival, disease free recurrence, overall survival, toxicity

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

Toxicity as per CTCAE and other scoring criteria (this will be in the national database and all patients will be invited to enter their own data into it)

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Uptake is increasing but still relatively slow due to the need to buy a machine and train the staff. I would imagine they could be offered on a supra regional network with one Papillon machine every 3 million or so patients. Though the patients most suited to it are the elderly who are not very fit to travel far to have a procedure.

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

☐ Most or all district general hospitals.

X☐ 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.

X☐ Minor.

Comments:

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?

No

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required 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:

[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).

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 which include investments in the healthcare industry	☐	**YES**
	X	**NO**
Do you have a **personal non-pecuniary** interest – eg 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?	**X**	**YES**
		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 lectured on the Papillon technique to groups of radiation oncologists and surgeons. I have taught other groups how to perform the technique. I do not believe this is prejudicial as I have presented the data available and the alternative treatments within these talks.

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

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

February 2010

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

Procedure Name:	**Contact X-ray brachytherapy (Papillon) for early stage rectal cancer (1234/1)**
Name of Specialist Advisor:	**Ayan Banerjea**
Specialist Society:	**Association of Coloproctology of Great Britain and Ireland**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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:

Contact radiotherapy can be used in more advanced stage rectal cancer, as an adjunct to standard external beam radiotherapy, as well as “early” rectal cancer. It may therefore be more appropriate to drop the “early stage” description and assess all applications of this treatment.

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:

This procedure is used in the management of rectal cancer.

The next two 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 which does this procedure, please indicate your experience with it:

X I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

Contact radiotherapy is often, but not always, used alongside surgery. I perform surgery – local and radical – in patients that may have had this treatment.

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:

I am part of our Colorectal Cancer MDT. I have also established our Early Rectal Tumour MDT and we have an established Contact radiotherapy service.

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

☐ I have undertaken bibliographic research on this procedure.

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

☐ I have undertaken 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 that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

None of the above apply.
This is not a new procedure but has not been practised widely in the UK. There is only 1 UK centre with significant experience. It is more than a minor variation on standard radiotherapy commonly used for rectal cancer in the UK.
There is published literature on Contact radiotherapy – but it is largely case series and dominated by data from continental Europe published by enthusiasts. There are no real safety concerns I am aware of. The exact role of Contact radiotherapy in the management of rectal cancer does need further evaluation.

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

Radiotherapy has an established role in rectal cancer but there are existing areas of uncertainty and considerable variations of practice nationally.
The role of long course chemoradiotherapy is well established but uncertainty surrounds the management of patients who respond completely to this treatment.
The role of short course radiotherapy is less clear – the MRC CR07 trial demonstrated improvements in disease control but no benefit in overall survival – perhaps due to the long term toxicity of radiotherapy.

Contact radiotherapy may have a number of different roles:

1. Treatment for early rectal cancer in those unfit for any surgical or endoscopic intervention – here the comparator would be External beam radiotherapy or "Best supportive care". In an ageing population, Contact radiotherapy has a role in treating patients who may otherwise receive no therapy or suffer more morbidity from standard radiotherapy.
2. Treatment for early rectal cancer in those who are fit but in whom radical surgery may be over-treatment. Here, Contact radiotherapy (often in combination with Transanal Endoscopic local excision) should be compared with both short-course radiotherapy + surgery and surgery alone. In this setting, standard surgery is radical resection: Anterior resection or abdominoperineal excision. However, the role of local excision is being

explored. Such comparison should include cancer disease-free survival and overall survival, but perhaps more importantly Quality of life measures that include stoma rates and urine, bowel and sexual dysfunction.

3. Contact radiotherapy can be used to boost long-course chemo radiotherapy given to rectal cancer not immediately amenable to curative surgical resection at the time of diagnosis and staging. Radiotherapy is given to improve resectability. This may yield a complete clinical response, the management of which is uncertain. The rates of complete clinical response to long course alone versus long course with a Contact boost may need comparison.

3.3 Please estimate the proportion of doctors in your specialty who are performing 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 4 UK centres with Contact radiotherapy established.

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

No deaths reported

No rectal perforation reported

2. Anecdotal adverse events (known from experience)

Poor healing and altered bowel control is commoner when any radiotherapy (Contact or standard) precedes any surgery (local or radical). Overall risks of iatrogenic morbidity are lower with Contact radiotherapy and/or local excision than the standard combination of external beam radiotherapy with radical surgery.

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

Adverse effects are largely consistent with those of standard radiotherapy: radiation proctopathy, altered bowel habit and rectal bleeding. Contact radiotherapy alone may yield fewer side effects than standard radiotherapy alone due to shorter wavelength of radiation and localisation effect – standard radiotherapy irradiates a larger field.

Contact ulcer is a specific complication which is often self-limiting.

Rectal bleeding may occur in the first 6 months (25%) but only 5% persist beyond that time or require treatment.

Infection and wound healing problems are known to increase when surgery follows radiotherapy – this is not specific to Contact.

Stenosis and fistula formation are recognised problems (quoted risk 1%) and more common when used in conjunction with local excision surgery.

Overall risks of iatrogenic morbidity are lower with Contact radiotherapy.

4.2 What are the key efficacy outcomes for this procedure?

See 3.2 – this treatment is used in different settings.

Disease control – local recurrence, distant recurrence, disease-free survival, overall survival.
Permanent stoma rate
Bowel, urinary and sexual function.
Quality of life.

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

Not all rectal cancers respond to this treatment initially and this cannot be predicted – also true of standard radiotherapy.
Long term control rates using this treatment requires wider study as current literature is dominated by enthusiasts.
There is wide variation in the use of radiotherapy for rectal cancer in the UK already – the role of Contact needs to be evaluated within this context.

4.4 What training and facilities are required to undertake this procedure safely?

I am unable to comment.

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

CONTEM	Prospective data collection registry
OPERA	RCT in development

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, e.g. PUBMED? (This can include your own work). If yes, please list.

No

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 about the role because of a lack of high-quality evidence. There are many unanswered questions currently about the role of radiotherapy in rectal cancer, and Contact radiotherapy is one branch of a wider debate. However, it is a promising modality that needs further evaluation in a few centres with good audit. The heterogeneity of patient factors, disease properties and treatment modalities shall make clean comparisons in randomised trials difficult to attain.

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):

Overall and disease free survival
Reduction of stoma/stoma complications
Reduction of complications from resectional surgery
Reduction of disturbance in:
- **Bowel function: continence and frequency**
- **Urinary function: continence and frequency**
- **Sexual function: impotence and sensation**

Faster return to normal activity
Lower rates of depression/anxiety/poor body image

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

Local recurrence
Systemic recurrence
Need for and complications of salvage surgery for local recurrence

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Slow until further evidence available.

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

☐ Most or all district general hospitals.

X 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:

Initially, this should be evaluated in a few centres only to clarify its role. Thereafter, between 10 and 20 centres will be required across the UK to provide adequate service provision.

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:

X Major.

☐ Moderate.

☐ Minor.

Comments:

Rectal cancer is common and early stage rectal cancer is becoming commoner due to Bowel Cancer Screening and better access to endoscopy. An ageing population shall yield a higher proportion of patients who are not fit for the current standard therapy but may yield benefit from local therapy such as Contact radiotherapy.

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

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required 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:

[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).

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 which include investments in the healthcare industry	☐	**YES**
	X	**NO**
Do you have a **personal non-pecuniary** interest – eg 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.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

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

February 2010

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

Procedure Name:	**Contact X-ray brachytherapy (Papillon) for early stage rectal cancer (1234/1)**
Name of Specialist Advisor:	**Prof Sun Myint**
Specialist Society:	**Association of Coloproctology of Great Britain and Ireland**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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.

X 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 standard of surgical care is surgery with APR for low rectal cancer and TME (AR) for mid and high rectal cancer. TEMS (Trans-anal Endoscopic Micro Surgery) can be offered for

T1 low rectal cancer <2cm. Patients need to be fit for anaesthesia as all surgical procedures need GA. Elderly patients or younger patients who are not medically fit should be offered contact X-ray brachytherapy (Papillon). In patients who are fit but refuse to have surgery should also be given an option of contact x-ray brachytherapy after MDT discussion.

The next two 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 which does this procedure, please indicate your experience with it:

☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

X I perform this procedure regularly.

Comments:

I have done over 800 patients over last 21 years.

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:

I get referrals from around the world (mainly from other centres in the UK). The cases are usually discussed at their local colorectal MDT and responsible clinician either surgeon or oncologist contact me to discuss suitability of their case for contact x-ray brachytherapy before they are referred to Clatterbridge. Since September 2011 Hull has started contact x-ray brachytherapy for the patients around their regional and have treated nearly 70 patients. Likewise, since April 2014 Nottingham and Guildford has started contacted x-ray brachytherapy and both centres have treated nearly 30 patients each. I refer patients to these centres where appropriate so that patients can have the treatment nearer their home (especially elderly patients or those with medical co morbidities)

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

☐ I have undertaken bibliographic research on this procedure.

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

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

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

X Other (please comment)

Comments:
We at Clatterbridge Cancer Centre has done many physics and clinical aspect device related research since Oct 2009. The machine has been modified and upgraded to improve safety and comfort for the patients based on our findings.
My colleagues Prof Jean Pierre Gerard (Lyon/ Nice) University of Nice (France) and Prof Robert Myerson from Washington University has undertaken some research including laboratory based research on this procedure. A small randomised trial from Lyon (Lyon 96-02) has been published in JCO in 2004. We are in the process of starting another International randomised trial OPERA which we hope to start shortly.

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 that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Contact x-ray brachytherapy (Papillon) has been in clinical use for over 80 years. The first publication from Berlin in 1936 and 1953 (Chaoul H. et al) set the scene. The 50 KV machine manufacture by Phillips is no longer available since the mid 1970's. A British company Ariane has produced an improved modern version of this machine and the prototype was first used at Clatterbridge in October,2009. We have now treated nearly 500 patients with this new machine. There are 10 centres around the world trained at Clatterbridge using this machine.

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

1. TEMS (Trans-anal Endoscopic Micro Surgery) but only indicated for T1 polyp cancer <2cm are suitable for this procedure.
2. TME (Total Mesorectal Excision) or APER (Abdomino Perineal Excision of the Rectum) are the standard of surgical care. However, surgical mortality and permanent or a temporary stoma rates are high.
3. EMR (Endoscopic sub-mucosal resection) or trans anal resection of polyps (TAR) on its own is not suitable for malignant polyps

3.3 Please estimate the proportion of doctors in your specialty who are performing 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:

See my comments for question 3

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

No known deaths related to this procedure.

No reported perforation in over 3000 patients treated in the past 80 years

No reported anal sphincter damage resulting in faecal incontinence

2. Anecdotal adverse events (known from experience)

Recto vaginal fistula occurred in <1% after surgical procedure (TEMS)

Rectal stenosis occurred <1% again after surgical procedure (TEMS) when contact x-ray brachytherapy is used as post-operative treatment for close resection margins in patients who refused completion surgery. Careful selection of patients and improve surgical techniques has reduced these complications in recently treated patients in the last 5 years.

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

The main side effect is bleeding caused by radiation induced telangiectasia which occurred in about 26% of cases. In most cases bleeding settle down after 12 -18 months. Those patients who are on anticoagulants or clopidrogel or Asprin needed Argon plasma coagulation in 5% of cases.

A preliminary report on toxicity of contact radiotherapy in first 100 patients treated by the new RT 50 Papillon machine. Sun Myint et al ACPGBI meeting poster abst: PO81(Colorectal Disease)July 2013

4.2 What are the key efficacy outcomes for this procedure?

1. Avoids surgical death (14% in over patients 80 years and 25% in patients over 90 years)
2. Avoids stoma in 40% of cases
3. Avoids surgical complications and hospital stay.
4. Low cost to health care providers (Health Economic assessment prepared by University of Liverpool- due for publication in April 2015)
5. Cure in 90% of cases with T1 rectal cancer
6. Cure in over 80% of cases with T2 rectal cancer
7. Improve quality of life by avoidance of surgery and stoma.

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

This treatment procedure do not treat lymph nodes. Therefore careful case selection is important. For early stage rectal cancer, the risk of lymph node spread is small. If there is uncertainty about lymph node status, external beam radiotherapy can be used in addition to contact x-ray brachytherapy.

In cases not responding to contact x-ray brachytherapy TEMS can be offered for small residual disease.

In more advanced cases (T3a or T3b) contact x-ray brachytherapy alone is not suitable as there is higher risk for nodal metastases. External beam radiotherapy is offered initially to down size and down stage the tumour. The small residual tumour is treated by contact x-ray brachytherapy boost to improve local control. We adopt a close watch policy and salvage surgery is offered for local relapses. In this way many elderly patients with low rectal tumour are spared surgery with permanent stoma which is offered only to patients (10-15%) who do not respond initially or relapses at a later date.

The data on 380 patients treated at Clatterbridge from 2003-2012 is due for publication shortly

4.4 What training and facilities are required to undertake this procedure safely?

Clatterbridge Cancer Centre holds regular Papillon training courses since 2010. Over 20 centres around the world has been trained and 10 centres have started treating patients (4 centres in UK; 3 in France; 2 in Denmark; 1 Switzerland) One centre in Sweden (Uppsala) has bought the machine and 4 more centres in the UK

(Devon, Newcastle, Oxford and Guys in London) are in the process of business case Submission.

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

1. OPERA trial which is an International randomised trial to evaluate the efficacy of contact x-ray brachytherapy is due to start shortly in France. In the UK approval from NCRI bagging & support has been applied (March 2015).
2. CONTEM observational studies (CONTEM 1 and CONTEM 3 are being prepared for publication shortly)
3. Health Economic evaluation of Papillon under taken by University of Liverpool is being prepared and due for publication in April 2015.
4. Plans for national registry of patients not included in the trials will be collected by University of Guildford data management team.
5. Main registry of all patients in the trials is kept by the data management team at University of Nice, France.

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, e.g. PUBMED? (This can include your own work). If yes, please list.

A special issue of 'Radiotherapy in early rectal cancer' was commissioned by Prof Peter Hoskin on behalf of the Royal College of Radiologists. This was edited by myself and all international experts involved in this field were invited to contribute to provide evidence for this procedure. The special issue was published in Clinical Oncology Volume 19; Number 9 (November 2007) [original publication submitted to NICE IP team]

Prof Jean Papillon and Prof Pierre Gerard has published several single institute results from France. Prof Sischy who introduced Papillon into the USA has published several papers to validate the results of Prof Papillon and Gerard. Cleveland Clinic, Mayo Clinics, University of Washington (Myerson et al.) and several other major centres in the USA has contact x-ray brachytherapy. Since the production by Phillips stopped many of these centres could not get spare parts to continue with this type of treatment.

All relevant publications not in PUBMED and data submitted to NICE IP team (Oct-Dec 2014)

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

The concept of rectal cancer management is changing among the experienced colorectal surgeons internationally in the last few years. Most surgical unit now practice 'Watch and wait' policy in patients who responded well to preoperative chemo radiotherapy and do not offer surgery immediately routinely. At least, most colorectal units now wait up to 10-12 weeks before offering patients surgery. In this way 20% of cases with rectal cancer who normally would have surgery routinely will be spared surgery as most experience colorectal surgeons are now more aware of

surgical harm in terms of surgical mortality and morbidity. (UK NBOCAP data and Rutten et al Lancet Oncology 2008)
Younger less experienced surgeons are reluctant to adopt this approach as this is not a standard of care. They would like to operate on all operable rectal cancer patients if possible.

Contact X-ray brachytherapy is mainly offered to elderly patients or younger patients with medical comorbidities who are at higher anaesthetic risk for surgery. However, some fit elderly and younger patients who are not keen on stoma or surgery have requested this treatment after they were offered radical extirpative surgery. Most experienced surgeons who practice 'Watch and wait 'policy in their respective units do not have any concern about offering contact x-ray brachytherapy for suitable patients (good responders after chemo radiotherapy) and adopt a 'Watch and wait' policy as they have experienced successful surgical salvage in cases of recurrences in small number of patients.
Younger surgeons with less experience has concerns about this approach.

NICE colorectal guidelines (2011) states clearly that:-

"Before starting treatment, offer all patients information on all treatment options available to them (including no treatment) and the potential benefits and risks of these treatments, including the effect on bowel function".

Patient's choice for their treatment is not offered in most colorectal units in the UK. Therefore, there is an urgent need to standardise the standard of care for rectal cancer taking into consideration:-

Age of the patient
Their fitness for surgery (PS)
Their wish to accept stoma (or not)
Process to refer patients to specialised units if there no specialist radiotherapy facilities available for rectal cancer in their local units

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):

1. **Organ preservation (preservation of rectum following treatment)**
2. **Avoidance of stoma**
3. **Avoidance of major surgery (APER or TME)**
4. **Local control**
5. **Quality of Life**

Survival will be similar for contact x-ray brachytherapy and surgery (APR or TME) as most recurrence can be salvage without compromising their survival.

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

Early complications- Radiation Proctitis (limited to 2-6 weeks)
- **Pain**
- **Rectal mucous discharge**

Late complications- Bleeding
- **Urgency**
- **Increase frequency of motions (External beam RT)**

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

The speed of diffusion of this procedure has already taken place nationally and internationally over the last 3 years. Many more centres are expected to start this facility shortly this year and this process is likely continue.

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

☐ Most or all district general hospitals.

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

Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:
Contact x-ray brachytherapy has been in clinical use for the past 80 years.
This procedure was in standard oncological text books including 'Oxford textbook of Oncology (Peckham, Pinedo &Veronese) 1995 OUP and DeVita Cancer Principles and Practice of Ocology (Lippincott).
Its safety and efficacy has been validated in many centres around the world.
The only drawback is the lack of randomised trial evidence. It was difficult to undertake a randomised trial as the number of patients suitable for treatment was small and very few centres specialised in this type of treatment. The only treatment machine made by Phillips became obsolete after mid-seventies.

1. There is revival of interest internationally in this treatment as more patients with early rectal cancer are now been diagnosed through "National Bowel Cancer Screening Programmes'
2. The recognition of surgical harm in elderly patients
3. There is increase in ageing population globally (3.3m above 85 years in UK alone)
4. Patients would like to avoid surgery and stoma ,if they were given a choice.
5. A low cost new British made machine is now commercially available
6. Many centres around the world has started using this machine.

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:

X Major.

☐ Moderate.

☐ Minor.

Comments:

1. Since the introduction of National Bowel Cancer Screening programme (NBCSP) in 2008 many rectal malignant polyps has been diagnosed. Malignant polyps 16% and Dukes A (T1 /T2) 25%.
2. There is increase in ageing population. Majority of the patients diagnosed with rectal cancer are above 65 years.
3. There is urgent need to reduce surgical harm (mortality 15-25% depending on the age)
4. There is urgent need to avoid stoma in treating early low rectal cancer
5. Patients wish to avoid surgery and stoma if possible but they were not given an option for their treatment as contact x-ray brachytherapy is not regarded by many surgeons as the standard of care.
6. There are potential 1000-2000 patients with early low rectal cancer suitable for contact x-ray brachytherapy
7. There is additional 1000 patients with more advanced rectal cancers (T3a/T3b) who can be down staged with chemo-radiotherapy (good responders).
8. Therefore, there is total of 2000-3000 potential patients who can benefit. Less than 300 patients are offered this treatment currently in the UK.
9. Cost of contact x-ray brachytherapy is low (~5K per treatment)
10. Potential savings for NHS in avoiding surgery and continuing cost of stoma care is considerable (Health Economics data currently prepared by university of Liverpool)

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?

We need minimum of 10 centres around the UK to provide contact x-ray brachytherapy. The cost of British made Papillon machine is ~300K (which is less than a fifth of a linear accelerator cost). This machine can be used for intra operative brachytherapy for breast as single fraction at the time of surgery for early screen detected breast cancer. No shielding is necessary for this machine and no special housing unit is necessary to operate this machine (Apart from usual radiation precautions of distant and time)
Avoidance of Surgery and stoma for 1000-2000 patients will save NHS considerable amount of money (Surgical cost 10-20K per patient depending on the procedure). The quality of life for the patients will improve and patients can be offered a choice for their preferred treatment.

In case of recurrence, salvage surgery can be offered without compromising their chance of cure. Many patients will avoid surgical deaths and complications. Cost savings to the NHs will be considerable.

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any

conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Consultancies or directorships attracting regular or occasional payments in cash or kind	**YES** **X**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	**YES** **X**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	**YES** **X**
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**
Investments – any funds which include investments in the healthcare industry	**YES** **X**
Do you have a **personal non-pecuniary** interest – eg 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**
Fellowships endowed by the healthcare industry	**YES** **X**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	**YES** **X**

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.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

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

February 2010

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

Procedure Name:	**Contact X-ray brachytherapy (Papillon) for early stage rectal cancer (1234/1)**
Name of Specialist Advisor:	**Jamie Mills**
Specialist Society:	**Association of Coloproctology of Great Britain and Ireland**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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

y Yes.

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

1.1 Does the title used above describe the procedure adequately?

y 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?

y Yes.

y 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:

Early rectal cancer is an evolving specialty, and it is clear to many that the traditional standard of an abdomino-perineal excision of the rectum or APER, or even a low anterior resection is an overtreatment for such an early tumour. This change in practice/ thinking can be likened to the change seen in breast cancer 15-20 years ago, and its evolution to considering breast conserving therapy over mastectomy, and all the quality of life benefits therein.

Against this back-drop of traditional surgery, is a changing landscape. Early rectal cancers are becoming more common through the Bowel Cancer screening program. The BCSP detects cancers at an earlier stage – up to a third may be a T1 or T2 (dukes A) .

Also, our patients are now older and living longer.

However major surgery in elderly patients comes with significant morbidity and mortality. Over the age of 80, a major rectal resection carries a 15-20% 6 month mortality with it.

Contact X-Ray brachytherapy, fundamentally is giving a monumentally large dose of radiotherapy to a very small area (the only reason we get away with it is that it is to a small area). The X-Rays are not very energetic so don't travel far into the patient. It can and does cure early rectal cancers.

It tests all non-oncologists belief that radiotherapy can and does cure cancer,- reliably. Most non oncologists struggle to believe that Radiotherapy will cure a cancer or when it does, it will do so with serious long term damage to the patient.

The assessment and judgement of suitability of a patient and their tumour for Contact X-Ray Brachytherapy is very important. Some tumours are simply too big (in length or circumfernetialness) or too thick to ever be cured by Contact therapy.

The other anxiety here is that Contact radiotherapy does not treat lymph nodes in the mesorectal fat. The risk of there being occult (unseen on MRI) lymph nodes in early rectal cancer ranges from 5% to 35%. These lymph nodes can be successfully treated with external beam chemo-radiotherapy.

The concept of treating early rectal cancer with local treatment (which may or may not include surgery) leaves many surgeons feeling uncomfortable. What if's arise – what if we miss an opportunity to cure? What if the cancer comes back and can't be cured at that point? What if it comes back and spreads? Also there may be fears that it will lead to a loss of specialism (if the surgeon doesn't do TEMS/ local rectal surgery), or a loss of minimum numbers to meet peer review requirements, and loss of activity in general.

The final point of anxiety here is less in the more elderly/ unfit people, but in younger, fitter patients. It would seem that yonger fitter patients have more to lose from/ when an attempt at cure with local treatment (Contact radiotherapy/ TEMS/ External beam chemo-radiotherapy) does not cure and a cancer returns. The person who has been doing this the most, and reporting outcomes– Angelita Habr-Gama (a Brazilian Surgeon) reports that around 70% of patients in her series are cured by chemo-radiotherapy without Contact / boost Radiotherapy. Of the 28 patients with recurrence, 26 could be operated on. So even if a cancer does recur after Chemo-radiotherapy there should be an excellent chance of still having successful cancer surgery (if the patient is fit enough to undergo said surgery).

The next two 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 which does this procedure, please indicate your experience with it:

☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

y I perform this procedure regularly.

Comments:

We regularly treat patient with contact radiotherapy, averaging 2-3 new patients a month. There is a mixture of patients – from those who are too unfit to undergo surgery where we are trying t cure/ delay recurrence. Then there are those with an early rectal cancer, and finally those patients who may be fit enough for a major resection but are choosing to trial a deferral of surgery (with close follow up)

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):

y I have undertaken bibliographic research on this procedure.

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

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

☐ 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):

y Established practice and no longer new.

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

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Has been being used since late 1970s!

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

The standard in fit patients depends on the stage. For T1 tumours the comparator would be TEMS +/- (chemo)radiotherapy or APER/ Anterior resection. For T2 tumours it would mainly be APER , though TEMS and (chemo) radiotherapy could be considered an emerging alertnative.

In unfit (for surgery) patients the comparator groups are radiotherapy or chemoradiotherapy.

3.3 Please estimate the proportion of doctors in your specialty who are performing 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.

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

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

See 2 and add rectal ulcer, stricture formation, fistulation/ rectal perforation.

2. Anecdotal adverse events (known from experience)

Symptoms of proctitis, tenesmus, rectal bleeding, looseness/ diarrohea, urgency, incontinence.

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

See above

4.2 What are the key efficacy outcomes for this procedure?

Complete clinical response. Local control rate. Local, loco-regional and distant relapse rates.
Cancer specific survival. Recurrence free survival.

Toxicity wise – incontinence (v rare indeed), proctitis Symptoms, rectal bleeding/ slime production.

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

2 things.

Firstly - and the largest hurdle is the understanding that radiotherapy will cure a cancer. There is basic Misunderstanding of the dose given in Contact therapy, and just how high it is. 90Gy in 3 fractions over 4 weeks is a phenomenal dose. Each fraction of Contact therapy being equivalent to at least an entire course (over 5 weeks) of external beam radiotherapy.

Secondly – the data that is present in the field is not of RCT standard. The main body of data are case series in the most, ranging from 50- 250 patients. That being said it has been being used for over 25 years now, since its creation by Papillion.

4.4 What training and facilities are required to undertake this procedure safely?

A contact radiotherapy machine, applicators and bed. All in an appropriately shielded room (to a diagnostic CT standard is ok).

Training requires the assembling of a team, radiographers, physicists, and oncologists to go and see patients being assessed, worked up for, and having the treatment in a centre currently delivering contact X-Ray brachytherapy. Any centre with reasonable through put is ok. Seeing a minimum of 10 procedures is necessary, and participating in 6+ would be recommended, before being proctored.

Following on this- proctoring by the host team would be required for the first 2-3 times the procedure is done. Ongoing support, and face to face meeting would be important following completion of the proctored cases.

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

CONTEMS 2,3 and 4.

OPERA is a trial currently being worked up by Prof S Myint, and is being considered by the NCRI Rectal group

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, e.g. PUBMED? (This can include your own work). If yes, please list.

no

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

Other than what has already been mentioned – no.

The treatment of early rectal cancer is an evolving field. There is uncertainty about how to go about local treatment in early rectal cancer.
Finally there is the oncologists/ Early rectal cancer MDTs judgement of suitability for the treatment. It takes a while for other clinicians to believe an individual/MDT are worthy of the referral when they are doing something new.

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):

Local control. Cancer or recurrence free survival.
Overall survival

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

local, reagional and distant recurrence rates.

Proctitis rates – all measures.

Incontience

Quality of life.

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

3-5 years

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.

y Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

I think there will need to be a balance between maintaining expertise/ numbers and avoiding patients travelling too far. This is after all a common cancer, and there will be no shortage of demand for it. So maybe more than 10, but definitely under 20 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.

y Moderate.

☐ Minor.

Comments:

Rectal cancer is common – 10-12000 cases a year in the UK. With screening, and the elderly population there will be a need to offer them a treatment they can cope with.

It will lessen the need for major resections, lessening the number of stomas (and stoma bags) people need a year. It will reduce (modestly) the number of major rectal resections occurring a year.

It will save costs/ bed days. It will save on all the difficulties that a locally advanced tumour brings – pain, district nurse vists, incontinence pads etc.

It should greatly ease suffering.

It will increase the need for MRI scans, and surfeillance/ f/up. The patient will have a better quality of life without stoma.

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

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required 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:

[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).

Consultancies or directorships attracting regular or occasional payments in cash or kind — **Y YES**

Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice** — **Y YES**

Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry — ☐ **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 — ☐ **NO**

Investments – any funds which include investments in the healthcare industry — ☐ **NO**

Do you have a **personal non-pecuniary** interest – eg 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? — ☐ **NO**

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

Fellowships endowed by the healthcare industry — ☐ **NO**

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

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

Comments:

I do private practice.
I have received honoraria from various Pharmaceutical companies for providing talks. Most recently this includes - Roche, Astellis, Ipsen, Sanofi, Johnson and Johnson and SiRTEX medical.
I am paid by Cancer Partners UK to offer specialist Radiotherapy advice, and other input into their Consultant Advisory Board.

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

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

February 2010

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.