NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

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

Please respond in the boxes provided.

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

Procedure Name:	IP780/2 Radiation therapy for early Dupuytren's disease
Name of Specialist Advisor:	Mr Bainbridge
Specialist Society:	**The British Society for Surgery of the Hand (BSSH)**

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

X☐ Yes.

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☐ Yes.

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

Comments: The management of Dupuytrens contracture is somewhat controversial. Hand surgeons have traditionally believed that they are the medical specialty best able to treat Dupuytrens disease. However this is a misunderstanding in the Dupuytrens disease is a genetic condition which is inevitably progressive and recurrent after treatment. The more invasive the surgery carried out the longer time interval until functionally significant recurrence occurs. This has led to a belief that bigger surgery is better but this is not a view that is endorsed by the majority of patients. Patients, particularly younger patients in their 40s and 50s, require a procedure that straightens the contracted finger or prevents progression of the early contracture with minimal time off work and away from hobbies and activities. There has therefore been a resurgence of interest amongst patients, more than surgeons, in treatments which delay or minimise the requirement for surgery.

Most plastic surgeons, especially, are used to considering radiotherapy in the context of high dose radiotherapy for tumour management. They are used to dealing with post radiation burns and post radiation scarring that makes the blood supply to the skin and subcutaneous tissues so poor and are quite rightly very worried about the possible impact of the side-effects of radiotherapy on non-malignant disease.

There is in addition in this country apart from keloid scars no history of the management of benign disease with radiotherapy. Even keloid scars are frequently not treated with radiotherapy if at all possible.

My understanding of radiotherapy for Dupuytrens disease after reading the literature in the English language from European authors and after discussion with British radiotherapists is that the dose of radiotherapy involved is extremely low and the type of radiation used has a very low penetration. I personally do not discuss the use of radiotherapy with patients. I take the view that it is something that I should mention to patients as a possible treatment option for the young patient with early disease or who has had early recurrence after previous surgery. I explain what the radiotherapy is, explain that I am not a radiotherapist and have no expertise or specific knowledge of the risks and complications and refer the patient to a radiotherapist who has experience in the management of benign disease with radiotherapy for further discussion and counselling.

The evidence from Europe is of moderate quality but would tend to suggest that on a population basis low dose radiotherapy will increase the time until functionally important contracture occurs when used in the primary disease and will similarly increase the time until functionally important recurrence occurs after surgical intervention.

I have had 4 or 5 patients who have had the treatment that I know about although I suspect there are several more. I have had one patient who after radiotherapy returned with progressive disease and the functionally important contracture at about the five-year stage and surgery was undertaken without

any problems. There was no evidence of delayed wound healing. We did give him 2 doses of antibiotics on a worst-case basis but there is no evidence that this was entirely necessary.

My personal feeling is that it is a treatment of moderate effectiveness with a modest to moderate evidence base that will be useful to some patients after appropriate counselling. I do not believe that it requires to be undertaken only as a part of a research study but I do believe that an NIHR funded research trial randomising patients to radiotherapy or sham would be a major step forward. However the observation post treatment would have to be for approximately 10 years.

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

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

☐ I have never done this procedure.

Comments:

I have never done the procedure as I am a surgeon rather than a radiotherapist

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

Comments:

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

☐ I have done bibliographic research on this procedure.

Comments:

3 Status of the procedure

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

☐ Established practice and no longer new.

Comments:
I do not believe that this is a new treatment. I believe that it is an established procedure which is routine in Europe and considered to be standard of care.

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

there is non-.

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

☐ Cannot give an estimate.

Comments:
I do know that many surgeons are very scared of radiotherapy for benign disease and refused to countenance the use of radiotherapy or refer patients

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

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

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

I personally refuse to discuss the details of the treatment with the patient all the complications all the risks. I have never trained as a radiotherapist, do no malignancy surgery at all and therefore have no current expertise in radiotherapy. I therefore would refer this question to a radiotherapist.

2. Anecdotal adverse events (known from experience)

the patients that I have operated on who have had appropriate low-dose radiotherapy from an appropriate expert do not appear to have any adverse events apart from mild dryness of the palms.

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

time to recurrence or progression of the Dupuytrens to a functionally significant contracture

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

the problem with radiotherapy for Dupuytrens disease is what area of the hand to treat. Dupuytrens can occur anywhere from the wrist crease distally. The first presentation of Dupuytrens with a nodule in the palm is not necessarily where the first functionally important contracture will appear will stop there is therefore a problem for the radiotherapist in do they treat the whole hand or do they just treat the visible stigmata of the disease. If they only treat the visible stigmata then it is highly likely that there will be progression of the disease outside the field of radiotherapy in a normal timeframe leading to a functionally significant contracture of another finger. This of course is not a failure of the treatment but a failure of the planning.

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

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

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

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

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.
There is very little agreement amongst the medical profession on what constitutes functionally important criteria in the progression of Dupuytrens. There are at least 2 competing patient reported outcome measures for Dupuytrens neither of which are ideal and neither of which are truly accepted and validated.

My personal view is that the only important measurement in Dupuytrens disease is the time until surgery or further surgery is required. However this is skewed by the fact that many patients who have undergone standard surgery are so traumatised that they will put up with a severely abnormal finger rather than undergo further treatment. Therefore the public does have to be an objective measure such as angle or a cut-off criteria in terms of patient reported outcome measure.

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

the Southampton score and the URAM are both available for the measurement of clinical outcomes. The SF-36 and other whole-body scoring systems are not sufficiently discriminatory for the follow-up of Dupuytrens. Systems where the patient nominates a functional problem can be used effectively but are more complex.

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

6 Trajectory of the procedure

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

I do not believe that it was spread quickly. I suspect less than 50% of patients that I refer to a radiotherapist actually end up undergoing radiotherapy. Over the last 2 – 3 years I have fully referred no more than 20 patients.

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

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

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:

☐ 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?

8 Data protection and conflicts of interest

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

8.1 Data Protection

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

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

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

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

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

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

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

[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 ☐ **NO**

Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice** ☐ **NO**

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 that include investments in the healthcare industry ☐ **NO**

Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic? ☐ **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 have referred private and NHS patients to one of the specialist radiotherapy practitioners in this country for consideration of radiotherapy and have received private and NHS referrals in return.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

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

Jan 2016

Conflicts of Interest for Specialist Advisers

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

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

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

2 Personal pecuniary interests

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

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

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

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

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

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

2.2 No personal interest exists in the case of:

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

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

3 **Personal family interest**

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

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

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

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

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

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

3.2 No personal family interest exists in the case of:

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

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

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

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

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

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

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

5 Non-personal interests

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

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

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

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

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

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Interventional Procedures Programme

Specialist Adviser questionnaire

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Please respond in the boxes provided.

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

Procedure Name:	IP780/2 Radiation therapy for early Dupuytren's disease
Name of Specialist Advisor:	Professor David Warwick
Specialist Society:	**The British Society for Surgery of the Hand (BSSH)**

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

☒ Yes.

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

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

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

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

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

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

Comments:

In my opinion having considered and discussed this matter, Hand Surgeons recognise that there may be a role in a very small subgroup with painful rapidly developing disease, perhaps with widespread sheets of disease. However, nodular Dupuytren's Disease is very common and usually does not progress. Wholesale use of radiotherapy will be very expensive, will expose patients to side effects (dry skin) and will reduce it availability for other more clinically relevant indications such as cancer. We need more data on its efficacy (placebo RCTs) and on the subgroups who may benefit.

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

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

☒ I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

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:

I very occasionally refer patients with widespread tender progressing plaques

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

☒ I have done bibliographic research on this procedure.

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

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

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

☐ Other (please comment)

Comments:

I edited the Federation of European Hand Society Instructional Course Book on Dupuytren's in 2015. This included a chapter on Radiotherapy. I have read in this topic before and have discussed widely with surgeon and also radiotherapists.

3 Status of the procedure

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

☐ Established practice and no longer new.

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

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Not so much novel- it has been available for a while- but in my view not quite yet established as a niche mainstream option.

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

Wait and See

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

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

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

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

☐ Cannot give an estimate.

Comments:

None in my speciality. Radiotherapists provide this treatment.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

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

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

2. Anecdotal adverse events (known from experience)

Dry palm

3. Theoretical adverse events

Carcinogenesis (but I would defer to the radiotherapists on this point)

4.2 What are the key efficacy outcomes for this procedure?

Progression of disease versus placebo to a clinically relevant condition. Cost is an essential outcome. Also longer term side effects.

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

How many of the target group would have progressed in the absence of treatment? Even if Dupuytren's does progress, with modern treatments such as meticulous surgery or collagenase (NB I have declared a Conflict of Interest on the latter) it is usually treatable so what is the benefit of earlier treatment unless a specific subgroup.

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

Defer to radiotherapists

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

Not to my knowledge.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.

Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please

do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

Not to my knowledge

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

None to my knowledge

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):

Resolution of pain; Angular deformity; Dupuytren's specific PROM

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

Dry skin

6 Trajectory of the procedure

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

Slowly due to very limited availability of equipment and limited subgroup to refer

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

☐ Most or all district general hospitals.

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

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

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

☐ Major.

☐ Moderate.

☐ Minor.

Comments:
Would be very major if all minor disease was treated.

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?

The radiotherapists perspective should of course be considered

8 Data protection and conflicts of interest

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

8.1 Data Protection

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

YES , understood

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

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

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

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

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

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

Comments:
Professor Warwick a been a paid Consultant to Pfizer and SOBI, European distributors of Xiapex. Xiapex (otherwise know as Clostridial Collagenase Hystiolyticum) is a treatment for Dupuytren's Disease. He has received travel support, accommodation and honoraria on several occasions in relation to advising on the drug, giving presentations to learned societies and other groups. He has no pecuniary interest or any other conflict with respect to Radiotherapy.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

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

[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).

Jan 2016

Conflicts of Interest for Specialist Advisers

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

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

2 Personal pecuniary interests

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

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

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

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

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

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

2.2 No personal interest exists in the case of:

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

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

3 **Personal family interest**

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

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

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

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

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

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

3.2 No personal family interest exists in the case of:

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

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

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

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

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

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

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

5 Non-personal interests

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

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

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

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

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

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

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

Please respond in the boxes provided.

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

Procedure Name:	IP780/2 Radiation therapy for early Dupuytren's disease
Name of Specialist Advisor:	Dr Shaffer
Specialist Society:	**The Royal College of Radiologists (RCR)**

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

☒ Yes.

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

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

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

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

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

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

Comments:

Most hand surgeons, with notable exceptions, do not routinely refer for this procedure.

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

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

☐ I have never done this procedure.

☐ I have done this procedure at least once.

☒ I do this procedure regularly.

Comments:

I treat approximately 5-10 patients per month for this

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:

I do get referrals from GPs and hand surgeons, but more than 50% of patients refer themselves to me, having heard about the procedure via patient forums or other informational sources.

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

☒ I have done bibliographic research on this procedure.

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

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

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

☐ Other (please comment)

Comments:

I took part in writing the Royal College of Radiologists document on radiotherapy for benign disease

3 Status of the procedure

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

☐ Established practice and no longer new.

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

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

This is a difficult question to answer, as it does not easily fall into any of those categories. There are those, including myself, who believe that evidence shows that radiation is effective in preventing the formation of contracture. There are those who disagree, due to the less than ideal quality of the evidence, as there was no randomised control group in the main trial. However, it is routinely performed in both private and NHS settings, although it is not universally available on the NHS. It has been done since at least 2010 (when the NICE guidance was published).

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

Watch and wait

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

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

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

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

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

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

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

Grade 1 acute toxicity in 28% (2% grade 2); Grade 1 chronic toxicity in 14%

Acute grade 1 side-effects included skin redness, dryness of skin

Acute grade 2 side-effects included extensive erythema, moist desquamation, pronounced local swelling

Chronic grade 1 side-effects included dryness, desquamation, mild skin atrophy with slight subcutaneous fibrosis, very occasionally change in heat & pain sensation.

Chronic grade 2 side-effects – none

Source: Seegenschmiedt MH, Keilholz L, Wielputz M, et al. Long-term outcome of radiotherapy for early stage Dupuytren's disease: A phase III clinical study. In: Eaton C, Seegenschmiedt MH, Bayat A, et al. (eds). Dupuytren's disease and related hyperproliferative disorders. Springer 2012. 349-371.

2. Anecdotal adverse events (known from experience)

My experience has been very much in line with the adverse events as above

3. Theoretical adverse events

There is a theoretical risk of radiation-induced malignancy (RIC). A recent review stated:

Studies of adults with benign conditions exposed to IR slightly above background levels, such as patients with tuberculosis exposed to multiple fluoroscopies (average 77) during treatment, have shown no marked increase in skin cancer risk.[71] One factor known to increase the RIC risk is the extent of sun exposure to the skin, suggesting synergism between the carcinogenic effects of IR and ultraviolet radiation.[90,91] The lifetime risk of development of a radiation-induced basal cell carcinoma (BCC) has been estimated to be approximately 0.006% based on 100 cm^2 of skin treated to a mean dose of 3Gy.[92] Another report has suggested this risk to be #0.1% in a sun-exposed field and an order of magnitude lower in skin not exposed to the sun.[90] It should be noted that all these figures are very much smaller than the spontaneous lifetime risk which is .20%.[92] Overall, the data suggest there is a dose-dependent increase in the risk of NMSC. Most of these are BCCs that can usually be treated successfully (Table 2), although some studies suggest that BCCs resulting from IR exposure are more aggressive and should ideally be excised with wider margins.[93] Long-term surveillance and reporting of suspicious changes in irradiated skin is advised, especially in individuals treated as children.

It should be noted that there are no case reports of the development of such RIC in the literature, and that another estimate of the risk e.g. for a 50 year old man was 0.04% on the Dupuytrens website (http://www.dupuytren-online.de/downloads/Risk%20of%20cancer%20with%20radiation%20therapy%20of%20Morbus%20Dupuytren.htm). Overall, it is clear that the risk is very low. However, I do discuss this more carefully with younger patients e.g. below the age of 40 years old.

4.2 What are the key efficacy outcomes for this procedure?

I have copied the outcome of the literature review from the RCR document below:
There are many retrospective studies in the literature going back many decades that have indicated the efficacy of radiotherapy for Dupuytren's disease 10-15. However, their usefulness is generally limited by baseline differences in patients and disease characteristics, radiotherapy doses and fractionations, definitions of endpoints, and short follow-up periods. The staging of Dupuytren's disease is illustrated in Table 1, where stage N is disease with no contracture, stage N/I is disease with up to 5 - 10 degrees of contracture, and subsequent stages indicate disease with more severe contracture.

Table 1: Staging Classification of Dupuytren's disease[16,17]

Stage	Clinical symptoms	Extent of extension deficit
N	Nodules, cords, skin retraction etc.	None
N/I*	As stage N + deformity of fingers	1 - 10˚
I	As stage N + deformity of fingers	11 - 45˚
II	As stage N + deformity of fingers	46 - 90˚
III	As stage N + deformity of fingers	91 - 135˚
IV	As stage N + deformity of fingers	> 135˚

*In some papers, N/I is defined as 1 - 5˚ of extension deficit.

A retrospective study with a median follow-up of six years looked at 96 patients (142 hands) 17. 70% had stage N or N/I disease. The patients were treated with 120 kV photons with a total dose of 30 Gy in 10 fractions, which was split into two phases of 15 Gy in 5 fractions over 1 week, with a six week gap between the phases. Overall, at last follow-up, 11% of hands showed stage progression, although 23% of those with at least 5 years follow-up progressed. Only minor side-effects were noted.

Similarly, a retrospective study with a median follow-up of 10 years looked at 99 patients (176 hands) treated with the same dose and fractionation (30 Gy in 10 fractions) and demonstrated progressive disease in 16% of patients with stage N, 33% in stage N/I, 65% in stage I, and 83% in stage II 18. A third study 19, with a median follow-up of 13 years looked at the outcomes of 135 patients (208 hands) treated with 30 Gy in 10 fractions (as above), and demonstrated progressive disease in 31% overall, with progression by stage of: N = 13%, N/I = 30%, I = 62%, II = 86%, III/IV = 100%. Additionally, it was noted that the outcome was significantly better if the disease was treated within one year of appearance of symptoms as compared with more than two years since the appearance of symptoms.

A prospective trial randomising patients between two dose levels (with no control group) looked at 129 patients (198 hands) 20. All of them had disease that had progressed within the last six months. Patients were treated with 120 kV at 40 cm FSD, with the aim to treat to a depth of 5 – 15 mm (down to the periostium of hand bones). The treated area was palpable disease with margins of 1 – 2 cm proximally and distally, and a lateral margin of 0.5 – 1 cm. Untreated areas were shielded with lead. Patients were randomised to two phases of 15 Gy in 5 fractions each (as above, with an eight week gap between the phases, total dose 30 Gy), or 21 Gy in 7 fractions, given on alternate days over a period of 15 days. The treatment was generally well tolerated, with acute grade 1 toxicity of 38% and grade 2 toxicity of 6%. There was a

chronic toxicity rate of 5% at 12 months. At 12 months follow-up, the overall treatment failure rate was 8%, with 2% needing corrective surgery. Progression by stage was: 0% in stage N, 3% in N/1, 15% in St 1, 40% in St II. There was no significant difference in efficacy or toxicity between the two dose groups.

A long-term follow-up of this study, published as a textbook chapter 21, looked at the outcomes of patients followed up for at least 5 years (median follow-up of 102 months). 406 patients (812 hands) were treated with radiotherapy, (total dose 21 Gy or 30 Gy (as above, although the gap between the two phases was quoted as 10-12 weeks), and a non-randomised control group of 83 patients (166 hands) consisting of patients who chose to be observed rather than treated. All had progressive disease in the last 6 - 12 months. Side-effects in the irradiated group were: Acute toxicity in 28% (2% grade 2); chronic toxicity in 14% (all grade 1). Acute and chronic toxicity rates were increased in the 21 Gy group compared with the 30 Gy group. Overall disease progression by stage was: stage N = 10%, N/I = 41%, I = 58%, II-IV = 89%. Regarding efficacy, significant reduction in disease progression and the need for surgery was demonstrated in both treatment groups compared with the control group, although there was no significant difference between the two treatment groups.

Table 2: Outcome of long-term follow-up of Seegenschmiedt study of radiotherapy for Dupuytren's disease[21]

Dose	Regression or stable disease (%)	Progression (all clinical signs, %)	Surgery (%)
Control (n=122)	38	62	30
21 Gy (n=293)	76	24	12
30 Gy (n=245)	80	19.5	8

References:

10. R Finney. Dupuytren's Contracture. *British Journal of Radiology* 1955; 28: 610-614.
11. Wasserburger K. *Therapie der Dupuytrenschen Kontraktur Strahlenther* 1956; 100: 546-560.
12. Lukacs S, Brain Falco O, Goldschmidt H. Raidotherapy of benign dermatoses: indications, practice, and results. *J Dermatol Surg Oncol* 1978; 4: 620-625.
13. Hesselkamp J, Schulmeyer M, Wiskemann A. Rontegntherapie der Dupuytrenschen Kontraktur im Stadium I. *Therapiewoche* 1981; 31: 6337-6338.
14. Kohler AH. Die Strahlentherapie der Dupuytrenschen Kontraktur. *Radiobiol Radiother* 25:851-853.
15. Herbst M, Regler G. Dupuytrensche K. Radiotherapie der Fruhstadien. *Strahlentherapie* 1986. 161:143-147.
16. Tubiana R, Michon J, Thomine JM. Evaluation chiffree des deformations dans la maladie de Dupuytren. In: Maladie du Dupuytren, monographies du G.E.G. Expansion Scientificque Francaise, Paris 1966.
17. Keilholz L, Seegenschmiedt MH, Sauer R. Radiotherapy for prevention of disease progression in early-stage Dupuytren's contracture: initial and long-term results. *Int J Radiat Oncol Biol Phys* 1996; 36: 891-897.
18. Adamietz B, Keilholz L, Grunert J, Sauer R. Radiotherapy of early stage Dupuytren disease. Long-term results after a median follow-up period of 10 years. *Strahlenther Onkol* 2001, 177: 604-610.

19. Betz N, Ott OJ, Adamietz B, et al. Radiotherapy in early-stage Dupuytren's contaracture. Long-term results after 13 years. *Strahlenther Onkol* 2010; 186: 82-90.
20. Seegenschmiedt MH, Olschewski T, Guntrum F. Radiotherapy optimization in early-stage Dupuytren's contracture: First results of a randomized clinical study. *Int J Radiat Oncol Biol Phys* 2001; 49: 785-798.
21. Seegenschmiedt MH, Keilholz L, Wielputz M, et al. Long-term outcome of radiotherapy for early stage Dupuytren's disease: A phase III clinical study. In: Eaton C, Seegenschmiedt MH, Bayat A, et al. (eds). Dupuytren's disease and related hyperproliferative disorders. Springer 2012. 349-371.

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

Yes. The Seegenschmiedt study above, whilst showing a very significant difference between the outcomes of the control and radiotherapy groups, did not have a randomised control group.

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

It could be done in any radiotherapy department.

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

No

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

no

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

no

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):

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

6 Trajectory of the procedure

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

It rather depends on what NICE decides. There is certainly a significant patient demand for this procedure, but it will depend on whether GPs and hand surgeons take on board any guidance that NICE give.

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

☐ Most or all district general hospitals.

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

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

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

☒ Major.

☐ Moderate.

☐ Minor.

Comments:
It is estimated that there are 1-2 million people in the UK with Dupuytren's disease. A subset of these will have progressive early disease, which is the only group that should be treated based on the available evidence. It is likely to involve large numbers of patients if the procedure is available nationwide.

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?

1. It may be that patients having surgical procedures e.g. needle aponeurotomy, may benefit from post-operative radiotherapy to prevent recurrence - a concept that is likely to be trialled in the US
2. There is often ectopic disease on the feet (histologically identical to Dupuytren's disease), also called Ledderhose or plantar fibromatosis, that can benefit therapeutically (regarding pain/function), and I would suggest including this in the guidance, as otherwise those patients will not get the benefit of this guidance. I will happily expand on this if it is thought relevant.
3. There are now several facebook patient groups that are advocating for the use of RT in Dupuytren's, indicating a strong patient demand.

8 Data protection and conflicts of interest

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

8.1 Data Protection

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

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

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

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

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

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

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

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

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

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

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

Comments:
I treat patients privately with radiotherapy for Dupuytren's disease and Ledderhose disease

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

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

Jan 2016

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

Conflicts of Interest for Specialist Advisers

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

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

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

2 Personal pecuniary interests

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

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

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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.

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

3 **Personal family interest**

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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

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

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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.

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- 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
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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

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Please respond in the boxes provided.

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

Procedure Name:	IP780/2 Radiation therapy for early Dupuytren's disease
Name of Specialist Advisor:	Mr Eckersley
Specialist Society:	**The British Society for Surgery of the Hand (BSSH)**

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

☒ Yes.

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

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

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

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

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

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

Comments:

This is a treatment with a clear divide in opinion between Hand Surgeons (and general orthopaedic surgeons who carry out Hand Surgery) and the Radiotherapists who offer this as a treatment. Most Hand Surgeons do not belive this is abeneficial treatment for patients with essentially a benign disease with huge variability in progression of the disease.

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

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

☒ I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

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:

I always mention the possibility of this treatment to my patients with palmar disease and suggest they investigate the potential risks and benefits themselves.

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

☐ I have done bibliographic research on this procedure.

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

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

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

☒ Other

Comments:

I have been involved in organising a symposium on Dupuytren's disease which included a presentation on Radiation therapy for Dupuytren's disease presented by Professor Seegenschmiedt from Hamburg a proponent of radiotherapy

3 Status of the procedure

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

☒ Established practice and no longer new.

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

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Established as in performed regularly in other countries but not in the UK where this would be considered a procedure of uncertain efficacy.

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

There are no comparators. This is a treatment that is proposed as reducing the rate at which Dupuytren's may progress. It is not a cure and cannot treat established contractures.

The comparator would be no treatment and observation

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

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

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

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

☒ Cannot give an estimate.

Comments:

This is a treatment not performed by Hand Surgeons. Would need to ask the Radiotherapy community.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

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

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

2. Anecdotal adverse events (known from experience)

The problems that I see after treatment are twofold. The first are the changes in the skin of the hand, where the skin becomes dry and often flaky. The loss of sweating can be important as sweating is a key component of grip. The second problem is that the patients are disappointed by the result when they went with established contractures and there is never any improvement.

3. Theoretical adverse events

Skin cancer. Adverse surgical outcome due to poor wound healing in irradiated skin

4.2 What are the key efficacy outcomes for this procedure?

Slowing progression of the Dupuytren's disease and so prolonging the time at which treatment for contracture may be necessary

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

As above. Do we know enough about Dupuytren's disease and its natural history to be able to absolutely state that it does slow the progression of the disease.

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

Not in my field. Presume you must be a trained radiotherapist

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

Not that I am aware of.

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

Not that I am aware of.

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 majority of patients with Dupuytren's disease in the NHS and Private Practice are seen by GPs and Hand, Orthopaedic and Plastic Surgeons and as a result very few are referred for radiotherapy as it is not widely known as a possible treatment.

5 Audit Criteria

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

There are none as the treatment is aimed at early disease where there are no accepted outcome measures.

Minimum is an audit of the effects of the radiotherapy on the hand in both the short term and long term to look at whether there are any skin or other cancers that arise at a greater rate than expected.

Need long term study on whether radiotherapy does slow down the progression of the disease. This almost certainly need as an RCT with a long term follow up.

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

Short term – Improvement in nodularity in the palm. Some patients have pain but Dupuytren's disease is not usually a painful condition so this must be interpreted with great caution.

Long term – Progression of disease to causing joint contracture.

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

Early- skin changes, including sweating with a loss of hand function. Affect on surgery (or collagenase) carried out to correct contracture which is not corrected by radiotherapy, in particular to skin graft take.

Late – Progression of disease despite radiotherapy
Skin or other malignancy

6 Trajectory of the procedure

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

I suspect very slowly as it is not well recognised and radiotherapy departments are probably busy treating cancer patients so access will be difficult

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

☐ Most or all district general hospitals.

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

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

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

☐ Major.

☒ Moderate.

☐ Minor.

Comments:

Mild palmar Dupuytren's disease is common particularly in the older population. I would suggest that if this group were to be offered this treatment it would be a significant burden on the NHS

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?

Radiotherapist views should be sought both those who offer this already and those who do not.

8 Data protection and conflicts of interest

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

8.1 Data Protection

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

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

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

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

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

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

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

Consultancies or directorships attracting regular or occasional payments in cash or kind	☒	**YES**
	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☒	**YES**
	☐	**NO**
Investments – any funds that include investments in the healthcare	☐	**YES**

[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).

industry	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☒	**YES**
	☐	**NO**

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

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

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

Comments:

I have in the past been paid an honorarium as an adviser to Pfizer when Collagenase first came to Europe and assisted in commenting on the introduction of Collagenase treatment for patients with Dupuytren's disease. I helped organize a conference on Dupuytren's disease at which all aspects of treatment where presented. Radiotherapy, Needle fasciotomy, Collagenase, and Surgery.

I am no longer involved and have no connection to SOBI, who took over from Pfizer as European distributors of Collagenase.

I am currently President of the British Society for Surgery of the Hand. This is a charitable society with the aim of promoting education, training and research into Hand Surgery to improve the quality of care offered to patients with hand conditions.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

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

Jan 2016

Conflicts of Interest for Specialist Advisers

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

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

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

2 Personal pecuniary interests

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

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

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

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

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

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

2.2 No personal interest exists in the case of:

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

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

3 **Personal family interest**

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

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

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

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

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

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

3.2 No personal family interest exists in the case of:

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

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

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

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

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

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

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

5 Non-personal interests

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

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

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

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

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