

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: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name: High-intensity focused ultrasound for glaucoma

Name of Specialist Advisor: Gus Gazzard

Specialist Society: Royal College of Ophthalmologists (RCO)

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

Yes.

1.1 Does the title used above describe the procedure adequately?

Yes.

Comments:

Also called 'ultrasound ciliary body ablation' by some surgeons.

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

Yes.

Comments: This is an alternative form of eye pressure (IOP) lowering by targeted destruction of the ciliary body.

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 done this procedure at least once.

Comments:

I have done this procedure 4 times.

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.

N/A

Comments:

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

I have had no involvement in research on this procedure.

Comments:

3 Status of the procedure

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

Definitely novel and of uncertain safety and efficacy.

Comments:

I have concerns about the lack of independent research used to sell this procedure.

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

Other forms of ciliary body destruction (e.g. 'cyclo-diode laser ablation') or other forms of eye pressure lowering surgery.

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

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

Comments:

Probably fewer than 1%

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)

Failure. Inflammation. Loss of vision. Pain.

Investigative Ophthalmology & Visual Science February 2015, Vol.56, 1089-1096.

doi:10.1167/iovs.14-14973

Cyclocoagulation of the Ciliary Bodies by High-Intensity Focused Ultrasound: A 12-Month Multicenter Study

Philippe Denis; Florent Aptel; Jean-François Rouland; Jean-Philippe Nordmann; Yves Lachkar; Jean-Paul Renard; Eric Sellem; Christophe Baudouin; Alain Bron

2. Anecdotal adverse events (known from experience)

Failure. Inflammation. Loss of vision. Pain.

3. Theoretical adverse events

Hypotony (too low an eye pressure);

4.2 What are the key efficacy outcomes for this procedure?

Preservation of vision and reduction in eye pressure.

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

There are concerns that it simply may not work as well as marketed.

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

Minimal, 5 minutes with a rep.

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

<https://clinicaltrials.gov/ct2/show/NCT01908985?term=hifu&cond=glaucoma&rank=3>

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).

A number of small scale posters at meetings, but not randomised.
Need to search the ARVO database.

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 some controversy that it is being marketed without independent RCTs.

5 Audit Criteria

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

IOP; Vision; re-treatments; treatment failure; number of medications used for IOP

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

IOP, mmHg
Vision, logMAR
Visual Field preservation

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Pain – up to 1 month
Inflammation – up to 1 month
IOP spikes >5mmHg
Loss of vision - any

6 Trajectory of the procedure

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

Slowly over 5 years, with likely a poor penetration across the profession.

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:

More would no doubt like to have it, but it will have limited uses.

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:

Moderate.

Comments:

Of course this depends on *how* safe it is.

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?

Conflicts of interests in all paper authors.

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.

YES 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 family¹ have a **personal pecuniary** interest? The main examples are as follows:

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 **YES**
 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 **YES**

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

Comments:

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).

- I have no *direct* conflicts of interest concerning this product but have worked with competing industry collaborations that might be used to treat similar patient groups .
- I am supported by an NIHR HTA grant to investigate Cost Effectiveness and Health Related Quality of Life in SLT.
- In the last 5 years I have been in receipt of research funding, honoraria, travel grant or related research-support from:
 - UCL Moorfields NIHR Biomedical Research Centre
 - Alcon, Allergan, Ellex, Glaukos, Ivantis, Lumenis, Merck/MSD, Pfizer, Santen, Thea
 - NIHR, MRC (for EAGLE trial), City University, Fight for Sight, British Council for Prevention of Blindness, Moorfields Eye Charity, Friends of Moorfields Charity, IGA-UK Royal College of Ophthalmologists
- Neither I, nor my family, have no financial interest in any ophthalmic product, company or related stocks but my brother works for Genentech, owned by Roche.

Thank you very much for your help.

**Dr Tom Clutton-Brock, Interventional
Procedures Advisory Committee Chair**

**Mark Campbell
Acting Programme Director
Devices and Diagnostics**

June 2018

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 Advisor 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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Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name: **High-intensity focused ultrasound for glaucoma**

Name of Specialist Advisor: Kin Sheng Lim

Specialist Society: Royal College of Ophthalmologists

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

Yes.

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

1.1 Does the title used above describe the procedure adequately?

Yes.

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

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

Yes.

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

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

Comments:

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

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

- I have never done this procedure.
- I have done this procedure at least once.
- I do this procedure regularly.

Comments:

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

- I have never taken part in the selection or referral of a patient for this procedure.
- I have taken part in patient selection or referred a patient for this procedure at least once.
- I take part in patient selection or refer patients for this procedure regularly.

Comments:

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

- I have done bibliographic research on this procedure.
- I have done research on this procedure in laboratory settings (e.g. device-related research).
- I have done clinical research on this procedure involving patients or healthy volunteers.

- I have had no involvement in research on this procedure.
- Other (please comment)

Comments:

3 Status of the procedure

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

- Established practice and no longer new.
- A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.
- Definitely novel and of uncertain safety and efficacy.
- The first in a new class of procedure.

Comments:

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

Diode laser such as external diode, Micropulse diode and Endoscopic Cyclophotocoagulation (ECP)

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)

Scleral thinning,

2. Anecdotal adverse events (known from experience)

induced astigmatism and post op persistent inflammation

3. Theoretical adverse events

Cystid macular oedema

4.2 What are the key efficacy outcomes for this procedure?

Poor, less than 15% reduction of pressure at 3 months from baseline (both wash-out pressure)

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

No randomised controlled trial. Only wash-out case series is from my unit. (result presented in ARVO 2018)

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

Not much

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

None

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).

The effect of Ultrasound cycloplasty (UCP) using High Intensity Focused Ultrasound (HiFU) on aqueous humor dynamics. Alaghband P, Galvis, E, Madekurozwa M, Bran Chu B, Overby D, Lim KS. ARVO Honolulu, April 2018

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

Promoted without any solid data to support it's use.

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). Please suggest the most appropriate method of measurement for each:

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Scleral thinning (one month), induced astigmatism (within one week), uveitis (after one month)

6 Trajectory of the procedure

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

Very slowly

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

- Most or all district general hospitals.
- A minority of hospitals, but at least 10 in the UK.
- Fewer than 10 specialist centres in the UK.
- Cannot predict at present.

Comments:

I don't think this product has any solid data to support it's use and there are also safety concern.

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:

I would not recommend it's use in 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?

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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Do you or a member of your family¹ have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind YES
x NO

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

Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry YES
x NO

Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences YES
x NO

Investments – any funds that include investments in the healthcare industry YES
x NO

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

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

Fellowships endowed by the healthcare industry YES
x NO

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

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

Comments:

I received a research grant from the company that manufacture this product in 2016. The study has now completed and we are now preparing the final report. Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair **Mark Campbell**
Acting Programme Director
Devices and Diagnostics

June 2018

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 - 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**

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- 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).
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- 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**

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- 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 Advisor 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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Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name: High-intensity focused ultrasound for glaucoma

Name of Specialist Advisor: Mr Leon Au

Specialist Society: Royal College of Ophthalmologists (RCO)

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

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

1.1 Does the title used above describe the procedure adequately?

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

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

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

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

Comments:

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

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

- I have never done this procedure.
- I have done this procedure at least once.
- I do this procedure regularly.

Comments:

I have been involved in HIFU from 2014 to 2016. During that time I've treated around 30-50 patients. I stopped the procedure afterwards as I was disappointed with the results and was concerned about some unreported side effects. I simply could not replicate the result that was initially reported by the Eyemust study in France. Recently I've learnt that the company has acknowledged the previous generations down fall and has launched a newer platform of HIFU, which delivers slightly higher energy to the ciliary body. Accordingly it should improve the efficacy but may increase the risk of complication too

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

- I have never taken part in the selection or referral of a patient for this procedure.
- I have taken part in patient selection or referred a patient for this procedure at least once.
- I take part in patient selection or refer patients for this procedure regularly.

Comments:

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

- I have done bibliographic research on this procedure.

- I have done research on this procedure in laboratory settings (e.g. device-related research).
- I have done clinical research on this procedure involving patients or healthy volunteers.
- I have had no involvement in research on this procedure.
- Other (please comment)

Comments:

3 Status of the procedure

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

- Established practice and no longer new.
- A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.
- Definitely novel and of uncertain safety and efficacy.
- The first in a new class of procedure.

Comments:

This is the first commercially available HIFU device designed to ablate the ciliary body, lowering eye pressure to treat glaucoma. It was first launched in UK 2014 as a treatment for refractory glaucoma (when previous glaucoma surgery has failed). Subsequently I learnt the company is expanding the indication to primary procedure (ie. First surgical treatment after drops have failed)

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

The closest would be cyclodiode photocoagulation which is an established treatment in glaucoma, especially refractory glaucoma, lowering pressure by ciliary body ablation. The HIFU was launched promising better efficacy and safer profile than cyclodiode although no comparison study was done (at the time anyway)

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)

Inflammation, macular odema, lack of clinical response requiring re-treatment

2. Anecdotal adverse events (known from experience)

I personally had problem with the HIFU between 2014 and 2016. The response rate was disappointing and a lot of patients pressure went back after short few months. Further more unexpected side effect occurred in the form of refractive change. Patient unaided vision reduced as a result of treatment induced astigmatism and myopia, although their best-corrected vision might be unchanged. This is something that can be hidden in published clinical trial. This is not an isolated incidence and has been confirmed with other HIFU user in the world, even with the current device and current users. Some of these refractive changes did resolve but after few months. Such refractive change is unusual amongst our current glaucoma surgical options

Second problem was it's effect on the pupil. There are reports of a fixed mid dilated pupil as a result of HIFU treatment, not just with the older version but with the new version. This was presented by it's user during a HIFU meeting in Manchester.

Thirdly I've experienced unusual macular odema with HIFU on my patients. Macular odema can occurred with ciliary body based treatment, but the odema I encountered was to a bigger extent that one would expect. I understand the current generation of HIFU uses even higher energy in the treatment in order to secure efficacy. This causes me concern as it might increase complication rate (again a message conveyed to us during a recent HIFU meeting in Manchester).

Lastly the HIFU device is quite large. It can be very difficult to fit it on to the eye when the patient has small palpebral aperture or tight lids. Eg. Oriental patients. I've had occasions failed to fit it on and had to abandon the procedure or convert to the conventional cyclodiode laser. Also in the company supplied description in your NICE email, it states it's a procedure that can be done in clinic room under any type of anaesthesia. In my experience the procedure is too painful to be done under topical anaesthesia. It requires a subtenon or peribulbar block, which can sometimes make the orbit even tighter making fitting of the HIFU cone tricky

I was concerned of the first generation HIFU during 2014-16 period due to lack of efficacy and unexpected side effect. The newer generation with higher treatment energy worried me enough that I chose not to try the machine again

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Pressure lowering effects, reduction in glaucoma medications

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

As stated above I did not see sufficient efficacy in terms of pressure lowering to justify continuing with HIFU. When it was first licensed to be used in refractory glaucoma, the IOP lowering was moderate at best and in that patient cohort (often with advanced glaucoma) the iop lowering effect was not sufficient.

As the technology is moved to primary procedure in milder glaucoma, although iop lowering effect does not need to be substantial due to the milder nature of the disease, the safety of it has to be good.

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

The correct size treatment cone needs to be selected to fit patient's globe size. This is now done by a preop biometry. Based on the biometric measurements one would select the correct cone size according to company provided chart. This also means each NHS hospital would need to either stock up on various sizes or pre-order them in advance.

Company and their distributor would provide training and support in the first few cases.

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).

Sheng Lim in St Thomas has recently finished his study on HIFU. HIFU acts on the ciliary body by ablating the ciliary processes, reducing aqueous production. However there has always been a claim that it might help to increase aqueous outflow too. Sheng Lim conducted his study and found no increase in aqueous outflow. He also found the decrease in IOP to be minimal and its entirely explained by aqueous reduction. This was presented in ARVO and recent ISGS meeting in Geneva

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

I've explained my personal concern with HIFU above. Please note this is entirely based on my own personal experience of the older generation HIFU back in 2014-16. Company has promised me aspect of this device has changed and efficacy has improved. I have no personal experience with the current version although the changes are not that substantial

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). Please suggest the most appropriate method of measurement for each:

IOP and medication reduction, need for subsequent re-treatment or glaucoma surgery

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

6 Trajectory of the procedure

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

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:

My personal view only based on my experience of this treatment

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 family¹ 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.

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).

Comments:

I've consulted for, done paid work or had expenses paid for by other glaucoma industry including Glaukos, Ivantis, Allergan, Alcon, Santen, Iridex, Visupharma, Thea

Thank you very much for your help.

**Dr Tom Clutton-Brock, Interventional
Procedures Advisory Committee Chair** **Mark Campbell
Acting Programme Director
Devices and Diagnostics**

June 2018

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 Adviser is responsible, but that is not received by the Specialist Adviser 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 Advisor 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.