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:	**Ultrasound-guided high-intensity transcutaneous focused ultrasound for the treatment of symptomatic uterine fibroids**
Name of Specialist Advisor:	David Cranston
Specialist Society:	British Association of Urological Surgeons (BAUS)

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:
Ultrasound-guided high intensity focused ultrasound (USgHIFU) is a novel modality for the treatment of solid tumours. Similar to diagnostic ultrasonography, it can be used as a non-invasive technique for treating solid tumours in internal organs such as the liver, kidney, pancreas, prostate and uterus.

As a novel modality, HIFU therapy does not belong to any speciality currently in clinical practice. Although I am a urological surgeon I am also the clinical director of the High Intensity Focused Ultrasound unit in Oxford and was responsible with colleagues for introducing this procedure to Oxford. The procedure is carried out by medical practitioners in various specialities. For instance, urological surgeons perform HIFU procedure for treating kidney and prostate cancer. Gynaecologists or radiologists carry out HIFU procedure for treating uterine fibroids. In Oxford, my colleague Professor Feng Wu, who is the first medical practitioner having GMC specialist registration on high intensity focused ultrasound since 2007, does most of HIFU procedures for uterine fibroids but only after referral from our gynaecological colleagues.

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:

My colleague Professor Feng Wu who is a HIFU consultant in Oxford University Hospitals does this procedure for uterine fibroids regularly. As a clinical director of HIFU unit in Oxford, I supervise him sometimes if he meets a difficult case.

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

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

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

x

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

Comments:

In Oxford, we have a multidisciplinary team that consists of gynaecologists, radiologists and HIFU specialists to work together for the treatment of patients with symptomatic uterine fibroids.

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:

In 2002, my colleagues and I established the first clinical HIFU Unit in UK. Since then, we have carried out Ultrasound guided HIFU (USgHIFU) clinical trials to investigate the safety, feasibility and efficacy of this novel treatment for various kinds of solid tumours, including kidney cancer, prostate cancer, liver cancer, pelvic tumour and uterine fibroids.

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:

Magnetic resonance image-guided transcutaneous focused ultrasound has been already approved by FDA for the treatment of uterine fibroids. NICE has also issued full guidance to the NHS in England, Wales, Scotland and Northern Ireland on magnetic resonance image-guided transcutaneous focused ultrasound for uterine

fibroids (IPG416).

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

Standard surgical procedure: Hysterectomy or Laparoscopic Myomectomy,

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:

As I explained above, HIFU therapy does not belong to any speciality currently in clinical practice. In Oxford urological surgeons like me carry out USgHIFU procedure for kidney and prostate cancer. However, we have a HIFU specialist (Prof Feng Wu) who used to a professor in surgical oncology perform USgHIFU procedure for patients with uterine fibroids.

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)

USgHIFU is relatively safe in the treatment of patients with symptomatic uterine fibroids, with a small risk of adverse events.

A study of 9,988 patients who had USgHIFU procedure reported that 1,062 patients (10.6%) presented with 1,305 adverse events. Based on SIR classification system, 1,228 (94.1%) complications were graded as Class A; 45 (3.4%) as Class B; 24 as (1.8%) Class C and 8 (0.6%) as Class D. They included increased vaginal discharge in 874 (8.75%) patients, lower abdominal pain in 225 (2.25%), leg/ buttock pain in 76 (0.76%), odynuria/hematuria in 52 (0.52%), skin burns in 26 (0.26%), uterus bleeding in 24 (0.24%), urinary retention in 16 (0.16 %), fever in 4 (0.04%), acute renal failure in 3 (0.03%), blurred vision in 2 (0.02%) and intestinal perforation in 2 (0.02%) [Chen J, et al. Ultrason Sonochem 2015; 27:671-676].

A non-randomised comparative study of 2,411 patients treated by USgHIFU (n=1,353) or surgery including hysterectomy (n=472) and myomectomy (n=586) reported that minor adverse events occurred in 335 (25%) patients in the HIFU group and in 719 patients (68%) in the surgery group (P < 0.001). The events recorded

included pain, weakness, or numbness in the lower limbs, back or perineum, haematuria, and general symptoms such as nausea and dizziness. The only categories where HIFU treatment had a higher percentage of minor complications than did surgery were superficial skin burns (2 versus 0), blurred vision and transient pain, and weakness or numbness in the back, shoulder, or lower limb, as shown in Table 1. Major adverse events attributable to the intervention occurred in 3 (0.22%) HIFU cases and in 133 (12.6%) surgical cases within 30 days after treatment. All three HIFU events were second-degree skin burns. Events in the surgery group included haemorrhage, infection, thromboembolic events, and injury to the bladder. There were three major events requiring readmission (vaginal cuff bleeding and abdominal distension) in the hysterectomy group. Major events were slightly less frequent in the myomectomy group (10.2%) than in the hysterectomy group (15.5%) [Chen J, *et al*. BJOG 2018 125:354-364].

Table 1. Comparison of adverse reactions in 2411 women with uterine fibroids allocated to treatment by high‐intensity focused ultrasound (HIFU) or surgery (myomectomy or hysterectomy)

Adverse event	HIFU group (n = 1353)	Surgery group (n = 1058)	Myomectomy group (n = 586)
Minor adverse event	335 (24.8)	719 (68.0)	397 (67.7)
Abdominal distension	0 (0.0)	4 (0.4)	3 (0.5)
Lumbar and back (sacrum) pain	150 (11.1)	134 (12.7)	64 (10.9)
Shoulder and back pain	0 (0.0)	11 (1.0)	11 (1.9)
Numbness and pain in lower limb	34 (2.5)	18 (1.7)	11 (1.9)
Weakness in lower limb	9 (0.7)	62 (5.9)	30 (5.1)
Pain and distension of anus	11 (0.8)	38 (3.6)	18 (3.1)
Subcutaneous emphysema	0 (0.0)	5 (0.5)	5 (0.9)
Uterine bleeding	88 (6.5)	222 (21.0)	150 (25.6)
Urinary retention	2 (0.15)	25 (2.4)	7 (1.2)
Haematuria	3 (0.2)	18 (1.7)	7 (1.2)
Fever (no therapy)	2 (0.15)	6 (0.6)	3 (0.5)
Respiratory tract infection	1 (0.1)	9 (0.9)	4 (0.7)
Fat liquefaction of incision	0 (0.0)	4 (0.4)	3 (0.5)
Incision infection	0 (0.0)	1 (0.1)	0 (0.0)
Skin burn (1st to 2nd degree)	2 (0.15)	0 (0.0)	0 (0.0)
Nausea and vomiting	21 (1.6)	158 (14.9)	80 (13.7)
Dizziness and headache	2 (0.15)	1 (0.1)	0 (0.0)
Blood pressure unsteadiness		1 (0.1)	
Blurred vision	10 (0.7)	0 (0.0)	0 (0.0)
Choking sensation in chest	0 (0.0)	1 (0.1)	1 (0.2)
Stomach pain	0 (0.0)	1 (0.1)	
Major adverse events	3 (0.2)	133 (12.6)	60 (10.2)
Intraoperative massive hemorrhagea	0 (0.0)	11 (1.0)	7 (1.2)
Intraoperative blood transfusion	0 (0.0)	96 (9.1)	41 (7.0)
Fever (>38°C)	0 (0.0)	3 (0.3)	2 (0.3)
Pelvic abdominal infection	0 (0.0)	5 (0.5)	3 (0.5)

Adverse event	HIFU group (n = 1353)	Surgery group (n = 1058)	Myomectomy group (n = 586)
Incision infection	0 (0.0)	3 (0.3)	1 (0.2)
Second - degree skin burn	3 (0.2)	0 (0.0)	0 (0.0)
Respiratory tract infection	0 (0.0)	2 (0.2)	1 (0.2)
Readmission	0 (0.0)	3 (0.3)	0 (0.0)
Deep venous thrombosis (lower limbs)	0 (0.0)	2 (0.2)	1 (0.2)
Vaginal cuff bleeding	0 (0.0)	1 (0.1)	0 (0.0)
Vaginal cuff infection	0 (0.0)	1 (0.1)	0 (0.0)
Drainage - site infection	0 (0.0)	1 (0.1)	1 (0.2)
Pelvic haematoma (drainage)	0 (0.0)	1 (0.1)	1 (0.2)
Pelvic abscess (drainage)	0 (0.0)	1 (0.1)	1 (0.2)
Bladder injury	0 (0.0)	1 (0.1)	0 (0.0)
Abdominal distension and vomiting (indwelling gastric tube)	0 (0.0)	1 (0.1)	0 (0.0)
Arrhythmia (emergency)	0 (0.0)	1 (0.1)	1 (0.2)

2. Anecdotal adverse events (known from experience)

None known

3. Theoretical adverse events

None other than above

4.2 What are the key efficacy outcomes for this procedure?

The key efficacy outcomes are relief of fibroid-related symptoms and improved quality of life in patients, as well as a size reduction in HIFU-treated fibroids on radiological images.

A recent publication in the British Journal of Obstetrics and Gynaecology with major input from Oxford reported a national non-randomised comparative study at 20 centres in China. A total of 2,411 patients were enrolled in the study, 1,353 in HIFU group and 1058 in surgery group, of whom 586 had myomectomy and 472 hysterectomy. The mean UFS scores improved successively from pre-treatment to 6 and then 12 months post-treatment for the HIFU and myomectomy groups, and the degree of improvement experienced was greater for HIFU patients than for surgery patients at both 6 ($p = 0.034$) and 12 months ($p = 0.001$). The QoL scores for both groups also improved successively, with the improvement in HIFU patients significantly greater at both 6 ($p = 0.001$) and 12 months ($p = 0.002$). Changes in the elements of the SF-36 scale showed a similar general trend towards progressive improvement over the 12 months after treatment in all groups. The HIFU group showed obvious improvements in physiological function, which were significantly greater than the changes in the two surgical groups. In the other seven components of the SF-36 measure, there were significant advantages for HIFU treatment in the

absolute improvement in bodily pain at 6 months, in vitality at 12 months and in emotional role at 12 months, but no other significant differences between the treatment groups at either 6 or 12 months [Chen *et al.* BJOG 2018; 125:354–364].

A non-randomised comparative study of 130 patients treated by USgHIFU (n=89) or laparoscopic myomectomy (n = 41) reported improvements in all Short Form-36 quality of life domains for both treatment groups during 12-month follow-up. Short hospital stay and time needed to return normal activities were better in the HIFU group than those in the myomectomy group (p <.001) [Wang F, *et al.* J Minim Invasive Gynecol 2014; 21:279-84].

A non-randomised control study of 166 women treated by the procedure (n=99) or by laparoscopic myomectomy (n=67) reported that both procedures improved the women's quality of life, with a shorter hospital stay and fewer adverse effects in women treated by HIFU [Liu Y, *et al.* BJOG 2017; 124 Suppl 3:36-39].

A case series of 76 patients reported that after USgHIFU treatment there was a significantly greater reduction from baseline in UFS-QOL score at 6, 12 and 24 months with a non-perfused volume (NPV) ratio of 80%. The volume of uterine fibroids was significantly decreased during 2-year follow-up. Four patients received repeated HIFU treatment [Wang W, *et al.* Eur Radiol 2012; 22:2553-2558].

A study of 272 women who underwent the procedure reported that both symptom severity score and UFS–QOL score were significantly improved with successive reduction in uterine fibroid volume during 12-momth follow-up [Lee JS, *et al.* Ultrason Sonochem 2015; 27:682-668].

A case series of 78 women who conceived after HIFU procedure (80 pregnancies) reported 19% (15/80) with natural delivery and 70% (56/80) with caesarean section. Miscarriage occurred in 4% (3/80) and 5% (4/80) were electively terminated [Zou M, *et al.* BJOG 2017; 124 Suppl 3:30-35].

A study of 131 nulliparous women who conceived after the procedure reported that of the 133 pregnancies. 26 (28%) women had natural delivery and 67 (72%) underwent caesarean section. 17 (13%) of the pregnancies ended in miscarriage and 4 (3%) were terminated at the request of the woman. On-going pregnancy occurred in 19 (14%) women [Li JS, *et al.* Sci Rep 2017; 7(1):3977].

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

None

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

Entry requirements of training course for HIFU operator: A senior SpR or consultant in either Radiology or Gynaecology. They have completed ultrasound imaging training course in Gynaecology and should have working experience in pelvic ultrasonography.

Trainees require attending a certified training course provided by HIFU training centre in hospitals and device manufacturers. The course involves theory and practice, as well as an extensive treatment guide. During the training period the trainees require to observe USgHIFU fibroid treatment procedure for at least 15 patients.

The trainees will be guided by senior HIFU operators on site for performing HIFU procedure. They require to be supervised for at least 20 patients before doing it alone.

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

I am not aware of any currently in progess but as stated above there have been many trial but the most important is the one outlined above by Chen *et al.* BJOG 2018; 125:354–364 in which Oxford had a major part to play.

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).

None other than those outlined above

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

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:

Outcome measures of benefit are as follows:

- Clinical outcomes: Using the uterine fibroid symptom and health-related quality of life questionnaire (UFS-QOL), symptom severity score and QOL scores are calculated pre-and post-procedure.
- Radiological outcomes: Using a contrast-enhanced pelvic MRI with gadolinium, the volume of HIFU-treated fibroids are measured on T2 weighted images and non-perfused volume is determined on contrast-enhanced T1 weighted fat suppressed image pre-and post-procedure.

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:

Adverse outcomes are as follows:

- Skin toxicity complication up to 1 day post-procedure
- Vaginal discharge or irregular bleeding complication up to 14 days post-procedure
- Lower abdominal pain complication up to 7 days post-procedure
- Bowel perforation complication up to 14 days post-procedure
- Sciatic nerve palsy complication up to 7 days post-procedure
- Rectum damage complication up to 7 days post-procedure

6 Trajectory of the procedure

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

If NICE issues full guidance on ultrasound-guided transcutaneous focused ultrasound for uterine fibroids, the use of this procedure will spread to the NHS in England, Wales, Scotland and Northern Ireland in five years.

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

☒ Most or all district general hospitals.

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

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Uterine fibroids are the most common pelvic tumours with an incidence in up to 70% of women over 40 worldwide. They are a significant cause of morbidity for women of reproductive age. Significant symptoms are reported in approximately 25% of cases who need to be treated with standard interventions such as Hysterectomy or Laparoscopic Myomectomy.

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:

Currently, many women wish to avoid more invasive interventions for symptomatic fibroids, and some of them choose HIFU procedure because they wish to preserve their fertility. Most patients with symptomatic uterine fibroids are suitable for HIFU treatment.

HIFU treatment is a non-invasive modality for patients with uterine fibroids, with less pain, short recovery time, no scarring and blood loss. Its influence on patient's condition and health is much less than surgical interventions. It is a day procedure under sedation rather than general anaesthesia. Patients do not need to stay in a ward after treatment.

The facility requirements for an USgHIFU device are much less than an operational theater.

Compared to standard treatments, ultrasound-guided HIFU will dramatically reduce the costing for fibroid treatment in NHS hospitals. It only requires one operator to perform the procedure.

Ultrasound-guided HIFU procedure is relatively safer in the treatment of patients with symptomatic uterine fibroids, with a small risk of adverse events.

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?

In the past decade the Oxford University Hospitals NHS Foundation Trust has successfully used ultrasound-guided HIFU treatment for cancer patients in clinical trials. With an approval by the Technology Advisory Group of Oxford University Hospitals, we have established a multidisciplinary team consisting of gynaecologists, radiologists, surgeons and HIFU specialists, and then used USgHIFU to treat 25 patients with symptomatic uterine fibroids. Our 2-year follow-up result demonstrates the clinical efficacy of HIFU ablation for uterine fibroids and the lower risk of complications. We believe that this non-invasive approach can offer an alternative therapy for women with symptomatic uterine fibroids.

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**

[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).

Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**
Do you have a **non-personal** interest? The main examples are as follows:		
Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

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

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

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 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

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Specialist Adviser questionnaire

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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:	**Ultrasound-guided high-intensity transcutaneous focused ultrasound for the treatment of symptomatic uterine fibroids**
Name of Specialist Advisor:	Dr Mo Hamady
Specialist Society:	British Society of Interventional Radiology

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

X☐ Yes.

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

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

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

Comments:

The procedure can be carried out using MR guidance and not only ultrasound guidance

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

x☐ Yes.

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

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

Comments:

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

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

☐ I have never done this procedure.

x☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

I do MRI guided focused ultrasound of the fibroids. I have not used ultrasound guidance for this purpose

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

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

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

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

Comments:

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

☐ I have done bibliographic research on this procedure.

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

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

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

☐ Other (please comment)

Comments:

3 Status of the procedure

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

☐ Established practice and no longer new.

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

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

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

Embolisation is the standard alternative procedure to open surgery for fibroids.

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

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

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

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

x☐ Cannot give an estimate.

Comments:

Very rare

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)

   skin burn. Bowel injury

2. Anecdotal adverse events (known from experience)

   same

3. Theoretical adverse events

   same

4.2 What are the key efficacy outcomes for this procedure?

percentage of devascularised fibroids, Improvement in quality of life, durability

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

uncertainty about patient's selection and durability

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

Special setting

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

Not 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).

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?

Yes

5 Audit Criteria

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

Quality of Life
Percentage of devascularised fibroids
Volume reduction (fibroids and uterus)
Duration of treatment session/ number
Complications

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:

Quality of life using UFS-QOL questionnaire
Changes in treated fibroids (devascularisation and volume)

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:

Skin injury/ bowel injury/ infection/ pain

6 Trajectory of the procedure

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

slow

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

☐ Most or all district general hospitals.

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

x☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

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

☐ Major.

☐ Moderate.

x☐ Minor.

Comments:

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.

xx☐ 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 ☐

☐ **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:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell Acting Programme Director

[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).

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 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.