

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Interventional procedure consultation document

# High-intensity focused ultrasound for symptomatic breast fibroadenoma

A fibroadenoma is a very common benign (not cancer) breast condition, the commonest symptom being a lump. If the lump becomes very large or painful, it can be removed using traditional or keyhole surgery. This procedure involves using high frequency sound waves that heat up the tissues in the lump. The aim is to reduce its size over time and possibly completely destroy it.

The National Institute for Health and Care Excellence (NICE) is examining high-intensity focused ultrasound for symptomatic breast fibroadenoma and will publish guidance on its safety and efficacy to the NHS. NICE's interventional procedures advisory committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The advisory committee has made draft recommendations about high-intensity focused ultrasound for symptomatic breast fibroadenoma.

This document summarises the procedure and sets out the draft recommendations made by the advisory committee. It has been prepared for public consultation. The advisory committee particularly welcomes:

- comments on the draft recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

**Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.**

The process that NICE will follow after the consultation period ends is as follows.

- The advisory committee will meet again to consider the original evidence and its draft recommendations in the light of the comments received during consultation.

- The advisory committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 23 June 2017

Target date for publication of guidance: 27 September 2017

## **1 Draft recommendations**

1.1 The evidence on high-intensity focused ultrasound for symptomatic breast fibroadenoma raises no major safety concerns. Evidence on its efficacy is inadequate in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to do high-intensity focused ultrasound for symptomatic breast fibroadenoma should:

- Inform the clinical governance leads in their NHS trusts.

IPCD: High-intensity focused ultrasound for symptomatic breast fibroadenoma

- Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's [information for the public](#) [*URL to be added at publication*] is recommended.
- [Audit](#) [*URL to audit tool to be added at publication*] and review clinical outcomes of all patients having high-intensity focused ultrasound for symptomatic breast fibroadenoma (see section 7.1).

1.3 Patients should be informed about all the alternative treatment options, which could include conservative treatment.

1.4 Further research should include publication of patient-reported outcome measures and studies with long-term follow-up.

## **2 Indications and current treatments**

2.1 Breast fibroadenomas are common benign masses that often develop during puberty, although they can occur in women of any age. The condition is rare in men. Simple fibroadenomas are usually 1–3 cm in size but giant fibroadenomas can be over 5 cm. They do not usually increase in size and some may disappear overtime. The condition is diagnosed by breast examination, and ultrasound or mammography. A needle core biopsy can be used for histological confirmation. Fibroadenomas are usually painless but can become painful and cause deformity.

2.2 If a fibroadenoma is asymptomatic, it does not need to be treated and no follow-up is necessary. However, any growth or other changes to the fibroadenoma should be reported. When symptomatic, fibroadenomas can be removed surgically or by

vacuum-assisted mammotomy, which can be done under general or local anaesthesia.

### **3 The procedure**

- 3.1 High-intensity focused ultrasound for breast fibroadenomas is a minimally invasive thermoablative technique that can be done at an outpatient clinic under local anaesthesia and sedation. A focusing ultrasound device delivers the treatment and allows for simultaneous regional monitoring. The technology uses sound waves that propagate through the tissues, generating local heat and inducing coagulative necrosis, protein denaturation and cellular destruction. A strong acute inflammatory response follows. Remodelling of the chronic inflammatory response lasts for up to 3 months and involves cellular regeneration, proliferation, migration and removal of debris.
- 3.2 Tumour size reduction should happen gradually with no need for further intervention.

### **4 Efficacy**

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a case series of 42 women (51 fibroadenomas) treated by high-intensity focused ultrasound (HIFU), 63% (29/46) of the fibroadenomas had reduced in size by 30% at 2 months, 67% (32/48) had reduced by 50% at 6 months and 87% (40/46) had reduced by 60% at 12 months. In a non-randomised controlled

study of 40 women treated by HIFU, fibroadenoma size was statistically significantly reduced by 17% at 2 weeks (standard deviation [SD] 19%,  $p=0.021$ ) and by 31% at 3 months (SD 53%,  $p=0.022$ ). In the same study, fibroadenoma size reduction was statistically significantly different in women treated by HIFU (44%, SD 39%,  $p=0.016$ ) compared with women in the control group (5%, SD 46%,  $p=0.53$ ) at 6-month follow-up; complete fibroadenoma reduction was reported in 33% (4/20) of women at 12-month follow-up. In a case series of 10 patients treated by HIFU, fibroadenoma diameter was reduced by 50% in 100% (10/10) of patients at 3-month follow-up. In a case series of 9 patients treated by magnetic resonance-guided HIFU, fibroadenomas size was reduced to 1.3 cm<sup>3</sup> (mean, SD 1.1 cm<sup>3</sup>) from a baseline of 1.9 cm<sup>3</sup> (mean, SD 1.5 cm<sup>3</sup>) in 50% (6/12) of women at 6-month follow-up.

- 4.2 In the non-randomised controlled study of 40 women treated by HIFU, 10% (2/20) of fibroadenomas did not change in size at 6-month follow-up.
- 4.3 In the case series of 9 patients treated by magnetic resonance-guided HIFU, technical failure was reported in 42% (5/12) of women.
- 4.4 In the case series of 42 women, 61% (31/51) of the fibroadenomas had caused discomfort before the procedure, which had resolved in 100% of the women at 12-month follow-up. In the same study, at baseline, 35% (18/51) of fibroadenomas were associated with pain, which had resolved in 100% of patients at 12-month follow-up. In the non-randomised controlled study of 40 women treated by HIFU, complete pain reduction was reported by 75% (6/8) of women at 6-month follow-up.

- 4.5 The specialist advisers listed key efficacy outcomes as reduction in lesion size, relief or resolution of symptoms, cost effectiveness, recurrence of symptoms in the short and long term, and time taken to do the procedure.

## 5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Discomfort or burning sensation assessed with a visual analogue scale (VAS, 0=no pain, 10=very severe pain) was reported by 90% (18/20) of women (mean score 6.4, standard deviation [SD] 3.2) in a non-randomised controlled study of 40 women treated by high-intensity focused ultrasound (HIFU). In the same study, persistent pain assessed with a VAS was reported by 10% (2/20) of women (mean score 1.6, SD 1.9) within 3 months of treatment. Pain during treatment was reported as being slight in 36% (4/11), moderate in 18% (2/11) and severe in 9% (1/11) of the procedures in a case series of 9 women treated by magnetic resonance-guided HIFU. In the same case series, mild pain was reported by 1 woman after the treatment of 1 fibroadenoma.
- 5.2 Numbness of the skin was reported by 1 woman of 20 in the non-randomised controlled study of 40 women treated by HIFU.
- 5.3 Superficial skin burn with blistering was reported in 6% (3/51) of fibroadenomas after the procedure in a case series of 42 women (51 fibroadenomas) treated by HIFU. A first degree skin burn was

reported in 1 woman of 20 in the non-randomised controlled study of 40 women treated by HIFU.

- 5.4 Hyperpigmentation of the skin was reported in 1 woman within days after the procedure in the case series of 42 women treated by HIFU. Hyperpigmentation of the skin was reported by 30% (6/20) of women at 3 months and 20% (4/20) at 6 months in the non-randomised controlled study of 40 women treated by HIFU.
- 5.5 Subcutaneous induration was reported in 1 woman of 42 at 12-month follow-up in the case series of 42 women treated by HIFU.
- 5.6 Ecchymosis was reported by 45% (9/20) of women in the non-randomised controlled study of 40 women treated by HIFU.
- 5.7 Erythema was reported by 30% (6/20) of women in the non-randomised controlled study of 40 women treated by HIFU.
- 5.8 Dimpling of the skin was reported by 1 woman of 20 in the non-randomised controlled study of 40 women treated by HIFU.
- 5.9 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed no anecdotal adverse events. They considered that the following were theoretical adverse events: poor cosmetic outcome, infection and severe fibrosis.

## **6 Committee comments**

- 6.1 Patients should have appropriate assessment in a breast clinic to exclude malignancy.
- 6.2 In the published evidence, there was a variation in treatment time, and patients reported pain or discomfort during the procedure.

## **7 Further information**

- 7.1 For related NICE guidance, see the [NICE website](#).
- 7.2 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and is developing an audit tool (which is for use at local discretion). This tool will be available when the guidance is published.

Tom Clutton-Brock

Chairman, interventional procedures advisory committee

April, 2017