National Institute for Health and Care Excellence

IP1520 – High intensity focused ultrasound for symptomatic breast fibroadenoma

IPAC date: July 2017

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Overseas health care professional		High intensity focused ultrasound is a safe procedure for symptomatic fibroadenoma. I am treating patients with fibroadenoma of any size with this procedure since 2012 and have treated over 70 patients in local anesthesia. Treatment Duration varies from 20 minutes to 60 minutes depending on the needed energy and the size of the fibroadenoma. We saw no relevant side effects yet. Shrinkage of the fibroadenoma was up to 95% after one year. Mean shrinkage was 65% and no patient qualified as a complete non-responder to date. Treatment effect regarding pain caused by the fibroadenoma occurred in over 90% of the patients.The alternatives are surgery or vacuum biopsy. All patients are counselled regarding these alternatives. In my opinion as a year-long user of this procedure high intensity focused ultrasound is an excellent non-invasive option for symptomatic fibroadenoma.	Thank you for your comment. The Committee very much welcomes hearing from professionals who have knowledge of the procedure. The consultee refers to his personal experience. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee, unless they contain important safety data.
2	Consultee 2 Patient		I would like to share my experience of having HIFU treatment and the reasons why I find it preferable over surgery. I wanted to have HIFU treatment for the treatment of multiple fibroadenoma because I was worried about being left with scars from surgery. I was worried that my breasts or milk ducts could be damaged from surgery and I also thought that having a less invasive surgery would be better than having anaesthetic.	Thank you for your comment. The Committee very much welcomes hearing from patients who have undergone this procedure and considered your experience and views in their deliberations.

			2 of my 4 lumps were treated via HIFU, one in each breast. The lump in my left breast was located in the 10 o' clock position and the treatment was painless.The doctors said they were able to perform a very good strong treatment. I remember it feeling warm and lasted approximately 45 minutes in total. Post surgery the lump swelled and the area went red in colour. Over time the lump gradually disappeared completely. I am left with a very slight discolouration on the skin where the lump used to be. The second lump was not as successful. The treatment was for a lump in the right breast in the 6 o' clock position. During treatment I felt intensive pressure on my chest, as if my chest was in a vice and the wind was being pushed out of me. The doctors reduced the intensity of the treatment and I did manage to finish it but I was very uncomfortable. Following treatment the area swelled like the left and was red in colour. The lump shrunk over time but did not disappear completely. I was still left with a smaller lump. I ended up having surgery on the 2 other lumps and the lump that was still present from HIFU treatment. I was quite worried about having surgery but it turned out to be ok. I was sore for a few weeks and found I had to be very careful to not move a lot and keep the wounds clean. I have been left with scars; 2 are very neat but one is thicker than I expected. Overall both treatments have left me with no lumps in my breasts. If both treatments using HIFU had gone as well in the right breast as it did in the left, I would have zero complaints. But, the right breast did cause me discomfort during treatment and I was disappointed that it did not result in the lump disappearing.	
3	Consultee 3		I have read with great interest your “IPP consultation document” as well as the special advisor input on the treatment of breast	Thank you for your comment.

	Overseas health care professional		fibroadenoma with HIFU. On your website you ask for further clinicians' input and I would be happy to do so. I do not consult in the UK, but in France. I hope that nevertheless my input will be helpful for you, as we have successfully performed HIFU for breast fibroadenoma for several years now at the [redacted])(results to be published). In your overview, I read that you didn't find any assessment done about this procedure. Please note that one has been recently done in France by the French National Health Authority (HAS). The HAS has given a positive evaluation to this assessment about to the breast fibroadenoma treatment with HIFU in the frame of the Forfait innovation (innovation reimbursement). The Forfait Innovation study, for which I am the principal investigator, will evaluate the cost-efficiency of HIFU compared to surgery in breast fibroadenoma (" the missing data") collecting real cost data and outcomes for both arms in a randomized study. Actually I am waiting the Health Ministry signature to start this study. Please find the pdf document attached hereafter (in French) plus a rough English translation in English of the document content. **English Translation of HAS Approval.pdf** **ac_2016_0076_favorable_forfait_innovation_echopulse_cd_2016_12_07_vd_2016-12-14_12-39-24_66.pdf**	Thank you for informing us of the assessment of HIFU for breast fibroadenoma by the French National Authority This was an approval for a study protocol to examine whether "the treatment of breast fibroadenomas by ultrasound-guided high intensity focused ultrasound (HIFU) is less expensive and as efficient as surgery" and not a Health Technology Assessment. Documents of this type would not normally be referenced in the overview. The results of the study once published as a peer reviewed article can be considered by NICE. The consultee refers to a non peer-reviewed study. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee, unless they contain important safety data.
4	Consultee 4 Overseas health care professional		I write this email in response to the public consultation period announcement regarding "High Intensity Focused Ultrasound (HIFU) for symptomatic breast fibroadenomas."	Thank you for your comment. Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected

			I am [redacted] of the [redacted] Breast Surgical Services at the [redacted]. As principal investigator, I recently completed a study evaluating HIFU for the treatment of breast fibroadenomas in the United States. This FDA approved study enrolled 20 patients and we hope to present the final results, including 12 month follow-up, at the 2017 annual meeting of the Radiological Society of North America. Early results from the study have demonstrated that the treatment is well tolerated, and appears effective at 9 months follow-up. This data has been presented at the 18th annual meeting of the American Society of Breast Surgeons on April 28th, 2017. Our group continues to work on the use of HIFU for the treatment of symptomatic breast fibroadenomas. I am currently the international principal investigator of what is hoped to be the pivotal study of HIFU for symptomatic breast fibroadenomas in the United States: (**https://clinicaltrials.gov/ct2/show/NCT03044054?term=focused+ultrasound+and+Brenin&rank=2**) This FDA approved study is currently open and enrolling at the [redacted] in New York. The study will open two additional sites in New York City, one at [redacted] Medical Center on June 12th and the other at [redacted] on June 19th. Target accrual is 100 patients, with criteria for enrolment being the presence of a symptomatic fibroadenoma resulting in significant patient distress. Please do not hesitate to contact me if you have any additional questions.	for presentation in the overview, unless they contain important safety data. The NICE IP team will review the guidance on HIFU for breast fibroadenoma if relevant peer-reviewed publications become available in the future.

5	Consultee 5 Patient		Hello, I have learnt that NICE was currently evaluating the echotherapy in the treatment of breast fibroadenoma and that in this process, I could share my experience as a patient. My name is [redacted], I am 30, [redacted]. I was diagnosed with two breast fibroadenomas 2 years ago and they were followed-up every 6 months since then. Lately, they became painful and avoided me to sleep on the side they were. My doctor advised me to have surgery as so far it is the standard of care. As I did not want to have surgery because of scars, hospitalization and recovery period, I started to look for alternative treatment. My doctor then informed me that a new therapy based on a technology which seemed to me something very novel at that time. I started to look for more information on the internet and found that echotherapy or so called HIFU was the only non-invasive alternative to surgery. From my point of view, it was the solution, without scars, without anesthesia, without hospitalization and with immediate recovery. I scheduled an appointment with a doctor to evaluate if I was a suitable patient for this procedure with the right indication. Hopefully, after having undergone elastography, the doctor confirmed that both of my fibroadenomas were indicated for HIFU. I had my fibroadenomas treated in the same session one month ago. The treatment took less than 1hour for both. I received a light anesthesia, the procedure went very well and I did not feel any pain neither during nor after the treatment. One hour after the procedure I could go back to my daily activities and the only recommendation was to take ibuprofen in case of pain. This was not necessary. A week after, I did a follow-up and check about the scars. There was nothing visible, and this was a relief. One month after, the fibroadenoma are not painful anymore, I can sleep now. The reason I share my experience with you is because I think it could be useful to other women in the same situation. HIFU was for me the only acceptable therapy for a benign tumor. It is much	Thank you for your comment. The Committee very much welcomes hearing from patients who have undergone this procedure and considered your experience and views in their deliberations.

			more constraint-less than surgery and I hope HIFU will keep on developing and become much more renowned. From my patient's point of view, HIFU should become the standard of care for fibroadenoma. Kind regards, [redacted]	
6	Consultee 6 Overseas health care professional		My name is [redacted]. I'm a breast dedicated radiologist working [redacted] Hospital of Paris and I would like to share with you my experience as part of a multicentric european trial and as a clinical user of HIFU Us guided treatment for fibroadenomas. I'll be honoured to respond all your questions and comments. With my best regards.	Thank you for your comment. The NICE IP team has considered comments from specialist adviser nominated by Professional Societies and Organisations during consultation the draft guidance is publicly made available for scrutiny.
7	Consultee 7 Overseas health care professional		My name is [redacted]: I am the head of the Experimental Senology at the department of womens health at the [redacted] I personally have no conflict of interest with [redacted] The [redacted] treats on yearly basis up to 700 primary breast cancer cases, diagnoses benign tumours and uses various techniques to address benign tumours such as surgery, HIFU ablation, vacuum assisted biopsy or cryo-ablation. I have used HIFU for BFA ablation since 4 years in 3 steps: first on clinical study for 27 patients for which I will add the main findings below and afterwards in standard use. Starting from July 2017 our center will be part of an international FDA approved study on symptomatic breast fibroadenoma. The technique which is very easy to use could be envisioned for clinical trials for selected breast cancer cases in the short-term future.	Thank you for your comment. The Committee very much welcomes hearing from professionals who have knowledge of the procedure. The consultee refers to his clinical and research expertise in using HIFU. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee, unless they contain important safety data. IP will routinely update guidance on a procedure given special arrangements every 3

			Having used this procedure for 4 years now, would like to add some comments: HIFU for breast fibroadenoma definitely is an innovative procedure and is less invasive for the patients compared to most other alternatives. Vacuum Assisted Biopsy of fibroadenomas is not CE Marked for use in therapeutic purposes nor reimbursed other than for diagnosis. Surgical excision or cryotherapy are the only comparator which makes sense. We observe a high patient satisfaction amongst our patients, as they appreciate the non-invasiveness of the method. HIFU is the only way to treat them completely non –invasively. In particular for women who develop multiple FA over the years, this is a method which avoids them having repetitive surgeries. We are currently finalizing the publication of the study for which I am confidentially sharing with you the main findings – please see below. High Intensity Focused Ultrasound (HIFU) for the treatment of symptomatic breast fibroadenoma with histological assessment at one year follow-up The Tuebingen HIFU trial was a prospective, mono-center, non randomized, open label trial. From December 2013 until November 2014, 48 patients were screened with FA, thereof 27 women were recruited into this trial and consecutively treated. Follow-up visits were performed at day 7 (D7), after 6 (M6) and 12 months (M12). A core needle biopsy was provided if an indistinct residual volume was visible after 12 month on ultrasound (US). 27 patients with symptomatic FA agreed to participate in the HIFU-trial and successfully underwent the HIFU treatment. Of these 27 patients 23 (85%) had a palpable lump, 16 (59%) presented pain and 19 (70%) reported anxiety related to the presence of the lump.	years or sooner if new efficacy or safety data becomes available.

			The mean age was 28.9 years (SD 9.1 years, median 26, range 18 – 50 years). 13 patients had a previous treatment for FA, 8 of them (62%) on the ipsilateral side. The results of this trial demonstrate a reduction or total regression in fibroadenoma volume by more than 65% after 6 months in 70% of the patients and after 12 months in 89% of patients. Our results are showing in 70% (16/23) of the cases the conversion of the initially palpable FA to non palpable at M12. To our knowledge, this is the first trial with a core needle biopsy proven post-treatment histology result. The histological outcome at 12 months of follow-up confirmed the sonographic diagnosis as scar tissue or necrosis and absence of vital tissue in all but 3 cases (88%). Prof. Dr. [redacted] [redacted] Handy: [redacted]	

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."