NICE advice

Sonata system for diagnostic imaging and treatment of symptomatic uterine fibroids

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is the Sonata system. It is used for diagnostic intrauterine imaging and transcervical treatment of symptomatic uterine fibroids. Fibroids are benign tumours that develop within the uterine wall and are one of the most common gynaecological problems in the UK. NICE's interventional procedures guidance on transcervical ultrasound-guided radiofrequency ablation for symptomatic uterine fibroids recommends the procedure should only be used with special arrangements for clinical governance, consent and audit or research.
- The **innovative aspects** are that it is an incisionless treatment option that combines a high-resolution intrauterine ultrasound probe with a radiofrequency ablation handpiece in a single delivery system.

- The intended **place in therapy** would be in place of more invasive surgery such as hysterectomy, myomectomy, or procedures such as uterine artery embolisation in people with symptomatic uterine fibroids.
- The **main points from the evidence** summarised in this briefing are from 6 studies. This includes 1 systematic review and meta-analysis, 3 prospective single-arm cohort studies, a pooled subgroup analysis from 2 of these prospective studies and 1 retrospective single-arm cohort study. The studies included a total of 1,320 people with uterine fibroids (of whom 234 had treatment with the Sonata system). They show that Sonata may provide effective treatment of uterine fibroids, and that most people were satisfied with treatment. Sonata was not compared with any other treatment.
- **Key uncertainties** around the evidence or technology are that there is no long-term clinical outcomes data directly comparing the technology with standard care. Also, the efficacy of the technology in people who want to have children in the future is uncertain.
- The **cost** per procedure with the Sonata system is estimated by the company as £2,795 for an outpatient procedure or £3,403 for a day-case surgery (excluding VAT). The average cost of standard care, assumed to be myomectomy (open or laparoscopic) or hysterectomy, is estimated as £3,664 (based on NHS reference costs 2018/19).

The technology

The Sonata system (previously called VizAblate; Gynesonics, Inc.) is a system for the diagnostic imaging and treatment of symptomatic uterine fibroids, including those associated with heavy menstrual bleeding. The system consists of a reusable intrauterine ultrasound probe and a single-use disposable radiofrequency ablation handpiece with an introducer and needle electrode. These 2 components lock together to form a single treatment device. The intrauterine ultrasound probe is used to identify fibroids from within the uterus and guide the introducer and needle electrodes into one or more targeted fibroids. The radiofrequency ablation handpiece is used to deliver radiofrequency energy to the targeted areas to reduce the volume of the fibroids. The radiofrequency ablation handpiece also comes with proprietary graphical guidance software. This displays a real-time graphic overlay on the live ultrasound image to help guide treatment and target ablation zones.

Innovations

By being placed transcervically, the Sonata system allows incisionless treatment of fibroids without the need for general anaesthesia. The technology has been shown to treat a wide range of fibroids, some of which cannot be treated with current transcervical methods (for example, FIGO types 3, 4, 5, 6 and types 2 to 5 [transmural]) and need more invasive open or laparoscopic surgery. By avoiding the peritoneal cavity, treatment with the Sonata system can reduce risk and morbidity associated with invasive fibroid treatment, such as hysterectomy and myomectomy. The technology may reduce the length of stay in hospital compared with invasive fibroid treatment and allow people to return to normal activity and work sooner. More than half of the people in the SONATA trial returned to normal activity within 1 day (with an overall mean of 2 days).

Current care pathway

Asymptomatic fibroids do not need treatment. Symptomatic fibroids can be managed using a range of treatment options depending on fibroid size, number and location, as well as the person's desire to have children in the future. Treatment options for symptomatic fibroids include pharmacological treatment, hysterectomy (surgical removal of the uterus), myomectomy (surgical removal of the fibroids), uterine artery embolisation and endometrial ablation techniques. NICE's guideline on heavy menstrual bleeding provides further information about treatment.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on heavy menstrual bleeding
- NICE's interventional procedures guidance on uterine artery embolisation for fibroids
- NICE's interventional procedures guidance on magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids
- NICE's interventional procedures guidance on transcervical ultrasound-guided radiofrequency ablation for symptomatic uterine fibroids. It recommends that the procedure should only be used with special arrangements for clinical governance, consent and audit or research. This is because although evidence on the safety of the procedure raised no concerns, evidence on its efficacy was considered limited in quality.

Population, setting and intended user

The Sonata system is intended for diagnostic intrauterine imaging and transcervical treatment of symptomatic uterine fibroids, including those associated with heavy menstrual bleeding. Uterine fibroids (also called uterine myomas, fibromyomas or leiomyomas) are the most common benign tumours in women and are the leading reason for hysterectomy. Fibroids may be single or multiple and can vary in size from a few millimetres to 30 cm or more. They can be asymptomatic or cause symptoms including heavy menstrual bleeding, urinary incontinence, pelvic pressure or pain (NICE's clinical knowledge summary on fibroids).

The technology is intended as an alternative treatment to more invasive surgery such as hysterectomy or myomectomy, or to procedures such as uterine artery embolisation.

The Sonata system is used in secondary care as an outpatient procedure or day-case surgery. Treatment will be done by a consultant gynaecologist trained to use the technology. Training and support are provided free of charge by the company. Clinicians must attend a 2-hour theory and practical training session delivered by the company. The company also provides intraoperative support to theatre staff and gynaecologists during the early stages of use.

Costs

Technology costs

The single-use Sonata case kits (the consumable element used for treatment) cost £2,500 per unit (excluding VAT).

According to the company, the total cost per procedure with the Sonata system would be about £2,795 for an outpatient procedure or £3,403 for a day-case surgery (excluding VAT). This estimate includes the cost of healthcare professionals' time (sourced from Ang et al. 2016), hospital stay and consumables. The capital cost of purchasing the Sonata system is £84,800 (excluding VAT); the company will consider placement of the hardware based on a consumable usage agreement. If purchased, the system is expected to need annual servicing at a cost of 10% of the cost of the capital components. According to the company the Sonata system should last for a minimum of 5 years, but with regular servicing the company expects that the lifespan of the system will be much longer.

Costs of standard care

The average cost of standard care, assumed to be myomectomy (open or laparoscopic) or hysterectomy, is £3,664 (based on NHS reference costs 2018/19, using Healthcare Resource Group codes MA08A and MA08B). The company estimates that the costs for myomectomy (open or laparoscopic) and hysterectomy are about £5,374 (plus or minus £1,000), including healthcare professionals' time (sourced from Ang et al. 2016), hospital stay and consumables.

Resource consequences

According to the company, the Sonata system is currently being used in 3 NHS centres.

Assuming that only 1 treatment is needed, adopting the technology in the NHS has the potential to be resource releasing. This is by reducing procedural time and length of stay compared with more invasive procedures (such as hysterectomy, myomectomy and uterine artery embolisation), and allowing the transfer of cases from an inpatient setting to day-case surgery and outpatient settings. If done in an outpatient department, the Sonata system could help cut staff costs by removing the need for an anaesthetist. According to the company, the technology can also help reduce general consumable costs per procedure compared with open surgical techniques and uterine artery embolisation. No changes to facilities or infrastructure would be needed to adopt the technology.

Two studies evaluating the cost consequence of adopting the technology were identified:

- The INSPIRE study assessed the perioperative and 12-month health economic and clinical outcomes associated with hysterectomy, myomectomy, and sonography-guided transcervical fibroid ablation (TFA) using the Sonata system (Brooks et al. 2020a). The study reported that, compared with hysterectomy and myomectomy, treatment with the Sonata system was associated with significantly lower index procedure cost, complication cost, and length of stay. This contributed to a lower total payer cost over 12 months.

- The CHOICES study compared short-term resource use, facility costs, and perioperative patient outcomes between TFA with the Sonata system and myomectomy (Brooks et al. 2020a). The study reported that, compared with myomectomy, treatment with the Sonata system was associated with significantly shorter operating room time and length of stay. The average total mean facility costs for TFA procedure ($7,563) were significantly lower than those associated with myomectomy ($11,425; p=0.002), including inpatient, abdominal, or laparoscopic myomectomy (p<0.001).

Regulatory information

The Sonata system is CE marked as a class 2b medical device. It was originally CE marked in December 2010 as the VizAblate system. It was renewed for the successor product, the Sonata system, in March 2014.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Fibroids usually develop in people between the ages of 30 and 50 years, with the incidence increasing with age, up to the menopause. Fibroids are more common among people with an African or Caribbean family background. The fibroids also tend to be larger, more numerous, happen at an earlier age and are more likely to cause symptoms in these people.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

One systematic review and meta-analysis, 3 prospective, multicentre, single-arm cohort studies (FAST-EU trial, SONATA trial and OPEN trial) and 1 subgroup analysis from 2 of these studies (FAST-EU and SONATA), and 1 retrospective single-centre, single-arm cohort study (VITALITY study) are summarised in this briefing. The studies involved a total of 1,320 people with uterine fibroids (of whom 234 had treatment with the Sonata system).

Evidence from 2 studies (the SONATA trial and the OPEN trial) was generated using the Sonata system, while 2 studies (the FAST-EU trial and the VITALITY study) evaluated its predecessor device (VizAblate system). The company states that differences between the current Sonata system and its predecessor relate to improvements in the user interface and the imaging capability of the intrauterine ultrasound probe. No changes were made to the radiofrequency treatment device, or the software controls involved in delivering radiofrequency energy.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

Overall, the evidence suggests that the Sonata system is an effective option for the incisionless and transcervical treatment of symptomatic fibroids, including those associated with heavy menstrual bleeding. Data from the FAST-EU trial and the SONATA trial reported that using the Sonata system resulted in statistically significant reductions in total and perfused uterine fibroid volume, menstrual bleeding and symptom severity, and improved health-related quality of life. In the SONATA trial, there was a low rate of surgical reintervention during the first 12 months after treatment and no device-related adverse events were recorded (Chudnoff et al. 2019). The evidence base suggests that on average people return to normal daily activities between 2 and 4 days after the procedure and are generally satisfied with treatment. In the SONATA trial (Lukes et al. 2020) 94% of people were very, moderately or somewhat satisfied with treatment at 3 years. Data from the OPEN clinical trial suggests that using the technology has little or no risk of causing intrauterine adhesions (Bongers et al. 2019). Longer-term follow-up data from a small cohort of FAST-EU trial patients (Garza-Leal 2019) suggests that some of the clinical benefits of the technology (reduced symptoms and improved quality of life) can last more than 5 years after treatment.

All available evidence came from single-arm studies only, so direct comparisons with alternative treatments for fibroids cannot be made. Also, long-term data is from 2 studies: a retrospective study of follow-up data over 5 years from a small cohort of patients (n=17) from a single non-UK centre, and a prospective study (n=147) of 3-year follow-up data. Larger, longer-term head-to-head studies comparing the technology with standard care (that is, myomectomy, hysterectomy or uterine artery embolisation) in an NHS setting would be helpful.

In most of the studies, the treatable fibroids were limited to those that were between 1 cm and 5 cm in diameter, because these would normally be treated with 1 ablation only. However, data on the treatment of larger fibroids (over 5 cm in diameter) with Sonata is available (Shifrin et al. 2021). This study reported that Sonata is an effective single-stage treatment option for nonpedunculated submucous fibroids, and larger or deeper uterine fibroids (including fibroid clusters), for which hysteroscopic treatment is not suitable. In the SONATA study, 14.5% of fibroids (less than 5 cm in diameter) were treated with 2 or more ablations (Chudnoff et al. 2019). The efficacy of the Sonata system to treat larger fibroids (over 5 cm in diameter) using multiple ablations is less certain. Although the evidence base includes people with a range of fibroid types (FIGO type 1, 2, 3, 4, and 2 to 5 [transmural]), the studies needed at least 1 fibroid to have either indented or abutted the endometrial cavity. People with type 0 fibroids only (no myometrial involvement) were excluded from the studies.

Studies excluded people who may want to have children in the future, so the role of the technology for these people is less understood. The 12-month MRI data from the FAST-EU trial (Bongers et al. 2019) showed that treatment with the technology may preserve uterine wall integrity, and successful pregnancies after treatment with the Sonata system (or VizAblate) have been reported (Lukes et al. 2020; Miller et al. 2019; Garza-Leal et al. 2014; Bends et al. 2018). Further evidence is needed on how the technology may affect fertility for people who want to have children in the future.

Evidence generated using the current Sonata system comes from 2 prospective cohort studies (SONATA and OPEN trial), both of which were funded by the company. The FAST-EU and OPEN trials involved UK centres, which may increase generalisability to the NHS.

Shifrin et al. (2021)

Study size, design and location

Subgroup analysis of 197 people (534 treated fibroids) from 2 prospective clinical trials (FAST-EU and SONATA) who had submucous or large fibroids treated with the Sonata (or VizAblate) system.

Intervention and comparator

Sonata (or VizAblate) system, no comparator.

Key outcomes

In the study, 86% of people with submucous fibroids only and 81% of people with large fibroids (over 5 cm in diameter) experienced bleeding reduction within 3 months after treatment with the Sonata system. During the 12 months after the procedure, overall symptom severity and health-related quality of life showed sustained, significant improvements. MRI imaging of fibroids in the FAST-EU trial showed an average volume reduction of 68%. Among people with submucous fibroids only, the rate of surgical reintervention during 12 months of follow-up was 3.7% in the FAST-EU trial and 0% in the SONATA trial.

Strengths and limitations

The FAST-EU and SONATA studies are multicentre studies with prospective design. The FAST-EU trial included 2 UK centres, increasing generalisability to the NHS (although the UK cohort had a small sample size).

Both studies were single-arm, so direct comparisons with alternative treatment options cannot be made. Both studies were funded by the company.

Lukes et al. (2020), Miller et al. (2019) and Chudnoff et al. (2019)

Study size, design and location

Prospective, multicentre, single-arm cohort study (the SONATA trial) of 147 women before

the menopause (aged between 25 and 50) with symptomatic uterine fibroids who elected for transcervical fibroid ablation (TFA) treatment. Lukes et al. (2020) reported on the 3-year outcomes, Miller et al. (2019) on the 2-year outcomes and Chudnoff et al. (2019) on the 12-month outcomes.

The study included 22 investigational centres in the US (n=21) and Mexico (n=1). It was done under an investigational device exemption from the US Food and Drug Administration.

Intervention and comparator

Sonata system, no comparator.

Key outcomes

Four women were excluded from the full efficacy analysis set at 12 months because they reached menopause and were unable to provide a pictorial blood loss assessment chart diary at their 12-month visits. The study met its co-primary endpoints at 12 months (n=143, full analysis set), with 64.8% of women experiencing 50% or greater reduction in menstrual bleeding and 99.3% of women who did not have surgical intervention for heavy menstrual bleeding. The mean pictorial blood loss assessment chart score decreased by 38.9%, 48.4%, and 51.1% at 3, 6, and 12 months after the procedure, respectively ($p<0.001$). At 12 months, 95.1% of women had experienced a reduction in menstrual bleeding. The mean maximal reduction in fibroid volume per patient was 62.4% ($p<0.001$). Symptom severity and health-related quality of life scores significantly improved by 32.1 points and 43.7 points, respectively, at 12 months ($p<0.001$). On average, women reported returning to normal activity in 2.2 days, with more than half returning to normal activity within 1 day. There were 97% of women who were satisfied with treatment and 96.3% noted improvements in their fibroid symptoms at 12 months. No device-related adverse events (AEs) were reported. Two serious procedural-related AEs were reported in 2 women (1.4%) and nonserious procedure-related AEs were reported in 74 women (50.3%).

There were 85% of women enrolled who returned for follow up at 2 years. Compared with baseline, symptom severity statistically decreased from 55 (plus or minus 19) to 24 (plus or minus 18; $p<0.001$), health-related quality of life statistically increased from 40 (plus or minus 21) to 83 (plus or minus 19; $p<0.001$). EQ-5D scores statistically increased from 0.72 (plus or minus 0.21) to 0.89 (plus or minus 0.14; $p<0.001$). Over 2 years, surgical

reintervention for heavy menstrual bleeding was done in 5.5% of women. There was 1 pregnancy with a normal peripartum outcome. Indicators of work impairment because of fibroid symptoms significantly improved from baseline to 2 years (including missed work time, overall work impairment, and activity impairment). There were 94% of women who were satisfied with treatment at 2 years (75% very satisfied, 13% moderately satisfied and 6% somewhat satisfied).

There were 15 women lost to follow up during the trial, with 90% of women accounted for at 3 years (132 people out of 147). Compared with baseline, mean symptom severity scores decreased from 55 (plus or minus 19) to 22 (plus or minus 21), health-related quality of life increased from 40 (plus or minus 21) to 83 (plus or minus 23). EQ-5D increased from 0.72 (plus or minus 0.21) to 0.88 (plus or minus 0.16; all statistically significant with $p<0.001$). The 3-year rates of surgical reintervention for heavy menstrual bleeding calculated by the binomial and Kaplan–Meier methods were 9.2% and 8.2%, respectively. Surgical reinterventions included 10 hysterectomies and 1 endometrial ablation. All work productivity and activity level parameters improved significantly during the 3-year follow up. At 3 years, 94% of women were satisfied with treatment (71% very satisfied, 14% moderately satisfied, 9% somewhat satisfied).

Strengths and limitations

This was a multicentre study with prospective design and endpoints defined using set objective performance criteria. A relatively robust patient selection process may have helped to minimise confounding factors. The study included patient-reported outcomes.

This was a single-arm study, so direct comparisons with alternative treatment options cannot be made. The study was funded by the company and did not involve any UK centres, limiting its generalisability to the NHS. Treatment was limited to fibroids that were between 1 cm and 5 cm in diameter. Women who wanted to become pregnant in the future were excluded.

Brölmann et al. (2016) and Huirne et al. (2018)

Study size, design and location

Prospective, multicentre, single-arm cohort study (the FAST-EU trial) of 50 women (aged 28 or older) with uterine fibroids and heavy menstrual bleeding. The study was done across 7 centres in Mexico (n=1), the Netherlands (n=4) and UK (n=2). Brölmann et al.

(2016) reported on 12-month clinical outcomes and Huirne et al. (2018) reported on health utility scores during the 12 months after treatment.

Intervention and comparator

VizAblate system, no comparator.

Key outcomes

There were 50 women (89 fibroids) who had treatment with the VizAblate system. One woman was excluded from primary efficacy analysis because of unusable imaging results. At 3 and 12 months, perfused fibroid volumes were reduced from baseline by an average of 68% (49 women; 89 fibroids) and 67% (28 women; 43 fibroids), respectively. Total fibroid volumes were reduced from baseline by an average of 55% (49 women; 89 fibroids) and 67% (28 women; 43 fibroids), respectively ($p<0.001$ for all compared with baseline). At 12 months, mean menstrual pictogram scores and symptom severity scores decreased by 54% (n=48; $p<0.001$) and 55% (n=49; $p<0.001$), respectively. The mean health-related quality of life (HRQoL) scores increased by 277% (n=48; $p<0.001$). There were 4 women (8%) who had surgical reintervention within 12 months; all were 6 months after treatment.

There were 49 women who provided responses to the EQ-5D-3L. Data from 1 woman who conceived 3 months after treatment and gave birth at term was excluded from analysis. Overall, treatment with VizAblate was associated with an increase in health utility scores, from a mean of 0.745 at baseline, to means of 0.838, 0.852, and 0.914 at 3 months, 6 months, and 12 months, respectively. The change from baseline at 12 months was statistically significant ($p<0.001$). When stratified by country, the improvement in health utility at 12 months was statistically significant for both the cohorts in Mexico ($p<0.004$) and Holland (p value less than 0.003), but not for the UK cohort ($p=0.75$). After translating health utility values into quality-adjusted life years (QALYs), the overall cohort experienced an average of 0.85 QALYs in the 1-year period from baseline to 12-month follow up.

The preservation of uterine wall integrity 12 months after treatment with VizAblate was also assessed for the 29 women using baseline and 12-month MRI image data. This secondary analysis (the INTEGRITY study, Bongers et al. 2019) showed that there were no areas on the MRI that indicated loss of myometrial integrity compared with baseline.

Strengths and limitations

This was a multicentre and international study with 2 centres in the UK, increasing generalisability to the NHS. The study had a prospective design and consecutive recruitment of patients, reducing risk of bias. MRI results were reviewed by an independent core laboratory to reduce variability and bias in MRI image quality and interpretation. The study used a validated, and standardised tool (EQ-5D-3L).

This was a single-arm study, so direct comparisons with alternative treatment options cannot be made. Only 58% of eligible patients (28 people out of 48) had MRI at 12 months. Follow-up time was limited to 1 year, so long-term effects are unclear. Women who wanted to have a baby in the future or had fibroids larger than 5 cm were not included. Although the study included 2 UK centres, the UK cohort had a small sample size (n=6) and half of all missing values in the study were from the UK cohort. The UK cohort may have been underpowered to detect statistical differences in health utility from baseline to 12-month follow up. The effect of socioeconomic status on health utility results cannot be excluded.

Garza-Leal (2019)

Study size, design and location

Retrospective, single-arm, data-collection cohort study (the VITALITY study) involving 23 women aged 28 and over with heavy menstrual bleeding secondary to fibroids. The study was done at a FAST-EU study site in Mexico and included women who had previously been enrolled and treated in the 12-month FAST-EU trial.

Intervention and comparator

Vizablate system, no comparator.

Key outcomes

The study generated long-term follow-up information from 17 women (73.9%), with a mean follow up of 64.4 months (range 57 to 73 months). The mean symptom severity scores significantly decreased from 64.9 at baseline to 27.6 at long-term follow up (p=0.002). Mean HRQoL scores significantly improved from 27.2 at baseline to 76.0 at long-term follow up (p=0.0001). No surgical reinterventions happened through the first 3.5 years after treatment. Two hysterectomies were reported, 1 after 3.5 years after ablation and

another about 4 years after ablation. Overall, there was a 12% incidence of surgical reinterventions over an average of 5.4 years follow up. This corresponds to an event rate of 2.2% per year. Freedom from surgical reintervention at 1, 2, and 3 years was 100%, and, at 4 and 5 years, was 88.2%. One pregnancy happened, and this was within the first year of treatment. It led to a normal-term birth by elective repeat caesarean and has been reported in a previous case report (Garza-Leal et al. 2014).

Strengths and limitations

The study had a high (around 75%) patient long-term follow-up rate. Treatment was given by a single operator, which may have allowed consistent perioperative management among patients. HRQoL scores and symptom severity scores were recorded and used to complement data on surgical reintervention.

The study was limited by having a relatively small patient cohort. Because it was a single-centre study done in Mexico the generalisability of results to an NHS setting are limited. It was a single-arm study, so direct comparisons with alternative treatment options cannot be made.

Bongers et al. (2019)

Study size, design and location

Prospective, multicentre, single-arm cohort study (the OPEN trial) involving 37 people having transcervical radiofrequency ablation treatment for symptomatic fibroids. Everyone had at least 1 FIGO type 1, 2 or 2 to 5 (transmural) uterine fibroid. The presence or absence of intrauterine adhesions was assessed at baseline before treatment with diagnostic hysteroscopy and again at 6 weeks after ablation (second-look hysteroscopy). The study was done at 6 academic and community hospitals in the UK (n=1), the Netherlands (n=1), Switzerland (n=1), and Germany (n=3).

Intervention and comparator

Sonata system, no comparator.

Key outcomes

There were 50 fibroids with a mean diameter of 3.4 (plus or minus 1.8 cm; ranging from

1 cm to 8 cm) ablated. Of the 37 people enrolled, 35 completed the study follow up and 2 electively withdrew from the study before the completion of study follow up. There were 34 out of 35 people who had paired baseline and second-look hysteroscopies that could be evaluated by the independent readers. One person was excluded from the analysis because of an unevaluable hysteroscopy video. At 6 weeks, none of these hysterectomy videos revealed any formation of intrauterine adhesions after treatment with Sonata. This included 6 people with apposing fibroids, that usually have a substantial risk of forming adhesions after operative hysteroscopic treatment.

Strengths and limitations

This was a multicentre study with a prospective design. The study used independent reviewers for the assessment of baseline and post-treatment hysteroscopy videos. One of the investigational sites was in the UK, increasing the generalisability to the NHS.

This was a single-arm study, so direct comparisons with alternative treatment options cannot be made. The study was not intended to be statistically powered and it is not clear how many of the people included in the analysis were treated in the UK. The study was funded by the company and 2 of the authors were consultants for the company.

Bradley et al. (2019)

Study size, design and location

Systematic review and meta-analysis of prospective studies for radiofrequency fibroid ablation (RFA) in 1,283 people (median age: 42 years) with symptomatic uterine fibroids (treated between 2003 and 2018). It included a total of 32 articles: 19 on laparoscopic RFA, 8 on transvaginal RFA and 5 on transcervical RFA (TFA; using Sonata or VizAblate system). Included studies were done in Mexico, US, Canada, Germany, Italy, Korea, Latin America, Norway, Denmark, China, Spain.

Intervention and comparator

Laparoscopic, transvaginal or transcervical RFA.

Key outcomes

There were 19 out of 20 prospective primary studies (reported in 32 articles) that had

good or fair methodological quality. Across all 3 types of RFA delivery approaches the mean procedure time was 49 minutes. Procedure time was statistically different among RFA delivery approaches (laparoscopic, 73 minutes; TFA, 44 minutes; transvaginal, 24 minutes), when for all pairwise comparisons $p \geq 0.002$. The mean time to discharge, time to normal activities, and time to return to work were 8.2 hours, 5.2 days and 5.1 days, respectively. For TFA the time to discharge, time to normal activities, and time to return to work were 2.5 hours, 3.3 days and 3.6 days, respectively. At 12 months follow up, fibroid volume decreased by 66%, HRQoL increased by 39 points, and symptom severity scores decreased by 42 points (for all $p<0.001$ compared with baseline). The annual cumulative rate of reinterventions because of fibroid-related symptoms was 4.2%, 8.2%, and 11.5% over 3 years. The reintervention rate at 12 months was comparable among TFA (2.7%), laparoscopic RFA (3.8%), and transvaginal RFA (5.3%), when $p \geq 0.52$ for all pairwise comparisons. The conclusions of this meta-analyses were unchanged among several sensitivity analyses.

Strengths and limitations

The conduct, analysis and reporting of the review adhered to the preferred reporting items for systematic reviews and meta-analyses (PRISMA). Only prospective studies were included. The review included a large sample size and conclusions were unchanged in various sensitivity analyses. Among the 20 prospective primary studies in this review, which were reported in 32 articles, study quality was rated as good or fair for 19 of 20 studies.

The company provided funding for the study. There were insufficient studies to statistically compare RFA delivery types for several outcomes and it was not possible to determine whether RFA efficacy was influenced by fibroid type or volume because of concerns of aggregation bias. Only a few of the included studies had a follow up of longer than 12 months.

Sustainability

No sustainability claims have been made by the company.

Recent and ongoing studies

- Transcervical Radiofrequency Ablation of Uterine Fibroids Global Registry (SAGE). ClinicalTrials.gov identifier: NCT03118037. Status: suspended (last updated February 2021). Indication: uterine fibroid. Device: Sonata system. Estimated study completion date: December 2025.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Three out of 5 experts were familiar with this technology and 2 had used the Sonata system before.

Level of innovation

Most experts felt that the technology was a novel concept or design. The innovative aspects identified by experts were that it combines intrauterine ultrasound imaging with targeted radiofrequency ablation and offers a potential outpatient approach that could be applied in most hospitals. Alternative treatments for fibroids were identified by experts and included: medical therapy (gonadotropin-releasing hormone analogues), hysterectomy, myomectomy, fibroid embolisation, hysteroscopic resection of fibroids and MRI-guided focused ultrasound (MRgFUS). One of the experts regarded the Sonata system as a better alternative to open or laparoscopic myomectomy when suitable within a target patient group. One of the experts noted that because the Sonata system targets the fibroid only it may not be associated with the same risks as fibroid embolisation, such as premature menopause or emergency hysterectomy. MRgFUS was highlighted by 2 experts as an alternative incisionless technique to the Sonata system, with 1 noting that it also involves thermal-ablative destruction of fibroid tissue. It was noted that, compared with MRgFUS, the Sonata system has its own portable standalone ultrasound capability with no need for a pre-operative MRI scan. Some experts also identified that hysteroscopic tissue retrieval systems are competing technologies for treating small submucosal fibroids (usually less than 3 cm).

Potential patient impact

Experts stated that avoiding surgery, and its associated risks and prolonged recovery period, is a potential benefit for people having treatment with the Sonata system. One noted that people can return to work 48 hours after having treatment with the Sonata system compared with up to 6 weeks after abdominal myomectomy, which also leaves a large cosmetic scar on the abdomen, similar to a caesarean birth. One expert noted that, compared with uterine artery embolisation, the technology seems to have less negative effect on fertility and a lower risk of hysterectomy. People with fibroids who need a fertility sparing treatment or want to avoid surgery were identified by experts as those who would benefit most from the technology. Three experts noted that people benefitting from this treatment would have intramural fibroids, with 1 expert specifying FIGO type 2 to 5, another specifying FIGO type 3 and possibly type 4, and the remaining expert specifying a fibroid size of 3 cm to 5 cm. Another noted that they would be more inclined to use the Sonata system in people with fewer than 8 uterine fibroids. People at high risk of abdominal surgery because of obesity, previous surgery or anaesthetic problems were also identified. Most experts thought that the technology could change the current care pathway in some way. Experts noted that the technology could lead to less invasive treatment, shorter duration of hospital stays, lower risk of complications and a faster return to normal activities, but further evidence would be needed to support this.

Potential system impact

Potential benefits to the healthcare system identified by the experts were reducing the number of surgical procedures for symptomatic fibroids, decreasing theatre occupancy (both operating and radiology) and bed stays, and freeing up time on MRI scanners. Most experts agreed that the Sonata system could replace existing treatment in selected people only. One of the experts thought that the technology would be an addition to standard care. Most experts thought that the Sonata system could be more cost effective than surgical treatments. One of them noted that costs for the device are substantial and that overall cost-savings may only be realised if reintervention rates are shown to be low. Another noted the expensive disposable cost per procedure but added that the procedure needs minimal extra equipment and takes no longer than 45 minutes of operating with no assistance. One expert thought that the technology would have similar costs to standard care but noted that comparative data is lacking. All experts noted that training would be needed on how to use the technology. One expert highlighted that a good level of ultrasound scanning ability would be needed to use the device. None of the experts were aware of any safety concerns surrounding the technology. One of them noted the limited

long-term evidence for the technology, highlighting that long-term morbidity has not been yet studied.

General comments

According to some of the experts, the technology is currently being used at 2 UK NHS centres. Two of the experts said that the technology would be used initially in secondary care, with 1 adding that it is unlikely to be applied in primary care. The initial cost of the device and training needs were the main issues noted by experts that could prevent the Sonata system from being adopted. Apart from training needs, no other usability or practical aspects of the technology were identified. The 2 experts who have used the device before found it easy to use. Experts noted that evidence from comparative trials against standard care (laparoscopic or open myomectomy or hysterectomy), as well as other techniques used in the treatment of fibroids, such as intrauterine devices and hysteroscopic tissue retrieval systems, would be needed to address some of the uncertainties in the evidence base. Long-term follow-up data relating to subsequent pregnancy were also mentioned by some of the experts, as well as studies assessing postprocedural complications, the incidence of rare complications (such as perforation rate and thermal injuries) and the sizes of fibroids that are treatable using the Sonata system. One expert also noted a lack of evidence around methodological techniques for the procedure. One expert thought that about 25% of symptomatic fibroids could be considered for treatment with the Sonata system, adding that people wishing to maintain fertility or those with fibroids greater than 5 cm would not be eligible. Another said that the Sonata system would be suitable for 20% of their patients. However, the expert highlighted that many of their patients have large and numerous fibroids, and that in centres seeing people with smaller and fewer fibroids this percentage is likely to be higher. Two of the experts noted that, in their hospitals, around 40 or 50 people a year may be offered treatment with the Sonata system.

Expert commentators

The following clinicians contributed to this briefing:

- Mr Bruce Ramsay, consultant in obstetrics and gynaecology, Peterborough City Hospital, received training from the company and the hospital was provided with free devices to offer treatment to 6 patients using the Sonata system (October 2018 to May 2019).

- Mr Saikat Banerjee, consultant gynaecologist and minimal access reproductive surgeon, Addenbrooke's Hospital, was paid by Medtronic for a teaching course in 2018 and was a voluntary assessor for the Ligasure system (Medtronic) in 2017.
- Mr J A Mark Broadbent, consultant obstetrician and gynaecologist, Royal Free London hospitals, Barnet and Chase Farm Sites, is a consultant adviser on an ad hoc basis for Medtronic who own Truclear, a tissue retrieval system used for the removal of submucous fibroids.
- Dr Rajneesh Mathur, consultant gynaecologist and subspecialist in reproductive medicine and surgery, has received honoraria for advice and lectures, and support to attend scientific meetings from manufacturers of medicines used in fertility treatment, including Merck, Gedeon Richter, Ferring and Pharmasure (2001 to 2019).
- Mr Stephen D. Quinn, consultant obstetrician and gynaecologist, Imperial College NHS Trust, acted as a non-paid consultant for Gynesonics (2017 to 2019), primary investigator on the OPEN trial (trial funded by Gynesonics).

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