NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of hysteroscopic morcellation of uterine leiomyomas (fibroids)

Uterine leiomyomas (fibroids) are non-cancerous (benign) growths that occur in the womb and can be associated with heavy menstrual bleeding, and with problems becoming pregnant and during pregnancy. Hysteroscopic morcellation is performed with anaesthesia. A special instrument is passed through the vagina and through the neck of the uterus to cut the leiomyoma into small pieces (morcellation), which are then removed by suction.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in July 2014 and updated in January 2015.

Procedure name

- Hysteroscopic morcellation of uterine leiomyomas (fibroids)

Specialist societies

- Royal College of Obstetricians and Gynaecologists
- British Society for Gynaecological Endoscopy.

Description

Indications and current treatment

Uterine leiomyomas (also known as uterine myomas or fibroids) are benign tumours that develop within the uterine wall. They can be single or multiple. They are one of the most common gynaecological problems among women in the UK. They are often

asymptomatic but they can cause symptoms such as menorrhagia, intermenstrual bleeding, a feeling of pelvic pressure, pain, and urinary incontinence. They may also be associated with reproductive problems such as subfertility and miscarriage.

Treatment depends on whether the leiomyomas cause symptoms and on the woman's desire for future childbearing. Asymptomatic leiomyomas need no treatment. Depending on their size, number and location, symptomatic leiomyomas can be managed by hysterectomy (surgical removal of the uterus) or myomectomy (surgical removal of the leiomyomas). Smaller submucous leiomyomas can be removed by hysteroscopic resection. Uterine artery embolisation may also be used. Other treatments include endometrial ablation, using energy such as microwave or heat, which may be suitable for some leiomyomas. Hormone-based treatments may be used on a short-term basis to relieve symptoms, or to shrink the leiomyomas before surgery or other interventional treatment.

What the procedure involves

Hysteroscopic morcellation aims to remove leiomyomas during a single insertion of a hysteroscope into the uterus. This contrasts with traditional hysteroscopic resection of leiomyomas, in which the instrument is reinserted into the uterus multiple times. Hysteroscopic morcellation is intended to reduce the risks of traumatic injury to the uterus and the risk of inadvertent fluid overload associated with traditional procedures (because the procedure may be completed more rapidly). An intended advantage of the procedure over thermal ablation techniques is avoiding the risk of thermal injury.

Hysteroscopic morcellation of uterine leiomyomas is usually done with the patient under general or spinal anaesthesia, typically as a day-case procedure. A hysteroscope is inserted into the uterus through the cervix and saline is pumped thorough a small channel in the hysteroscope to distend the uterus. A specially designed morcellator is introduced via the hysteroscope and used to cut and simultaneously aspirate the morcellated leiomyoma tissue. The aspirated tissue can be collected for histological analysis.

Different devices are available for this procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to hysteroscopic morcellation of uterine leiomyomas. Searches were conducted of the following databases, covering the period from their commencement to 3 November 2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with uterine leiomyomas.
Intervention/test	Hysteroscopic morcellation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on approximately 208 patients treated by hysteroscopic morcellation from 2 randomised controlled trials (1 of which compares different treatment settings for hysteroscopic morcellation rather than comparing different treatments), 1 non-randomised comparative study, and 3 case series[1–4, 6,7]. In addition, there is a review of 119 adverse events related to hysteroscopic morcellation that were reported on the Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database, based on approximately 180,000 procedures[5].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on hysteroscopic morcellation of uterine leiomyomas (fibroids)

Study 1 Van Dongen (2008) – included in 2013 overview

Details

Study type	**Randomised controlled trial**
Country	The Netherlands
Recruitment period	2005–6
Study population and number	Women with intrauterine polyps or submucous myomas (type 0 or I). **n=60 (30 hysteroscopic morcellation [10 myoma] versus 30 conventional hysteroscopic resectoscopy [12 myoma])**
Age and sex	Mean age=49 years
Patient selection criteria	Intrauterine polyp or type 0 or type I submucous myoma smaller than 30 mm in diameter and an indication for removal (abnormal uterine bleeding, dysmenorrhoea, infertility). Exclusion criteria were type II myomas, suspicion of malignancy before surgery, or contraindications for hysteroscopic surgery.
Technique	All procedures were done in an inpatient setting with the patients under general or spinal anaesthesia. Hysteroscopic morcellator (Smith and Nephew, USA) was used with normal saline solution for distension and irrigation. Conventional resectoscopy used sorbitol (4%) for distension and irrigation.
Follow-up	**Not reported**
Conflict of interest/source of funding	Financial support was received from Smith and Nephew, USA.

Analysis

Study design issues: Randomisation was done using sealed opaque envelopes. The procedures were done by 6 residents in training for obstetrics and gynaecology. The primary outcome measure was the operating time, defined as the time between the introduction of the hysteroscope until the removal of the instrument at the end of the procedure. Intention-to-treat analysis.

Study population issues: There were no significant differences in baseline characteristics (age, median parity, menopausal state, indication for surgery, preoperative diagnosis, size of intrauterine abnormality) between the groups. Most patients had polyps rather than myomas – the results were not separated by indication.

Other issues: The authors noted that no learning curve was observed. They also noted that approximately 20% of resectoscopy procedures had to be taken over by the trainer, compared against 3% of the morcellator procedures.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **60 (30 versus 30)** **Mean operating time (minutes)** • Hysteroscopic morcellation=10.6 (95% CI 7.3 to 14.0) • Conventional resection=17.0 (95% CI 14.1 to 19.9), p=0.008 **Mean total distension fluid used (ml)** • Hysteroscopic morcellation=3413 (95% CI 2209 to 4617) • Conventional resection=5050 (95% CI 4106 to 5994), p=0.041 **Mean total fluid deficit (ml)** • Hysteroscopic morcellation=409 (95% CI 229 to 589) • Conventional resection=545 (95% CI 406 to 684), p=0.224 **Median number of insertions** • Hysteroscopic morcellation=1 (range 1–2) • Conventional resection=7 (range 3–50) Multiple linear regression analysis showed that operating time increased significantly, in both groups, when volume of intrauterine disorder increased.	1 patient allocated to conventional resectoscopy did not undergo the intended procedure because of a perforation during cervical dilation. Hysteroscopic morcellation was aborted prematurely in 1 patient with submucous type I myoma because of an imminent fluid overload. Histological analysis of the specimens revealed that 2 patients in the hysteroscopic morcellation group had malignant endometrial carcinoma (both were diagnosed with myoma type 0 before the surgery). Both patients were treated primarily with the hysteroscopic morcellator and subsequently underwent (after diagnosis) a radical hysterectomy with bilateral salpingo-oophorectomy.
Abbreviations used: CI, confidence interval	

Study 2 Emanuel MH (2005) – included in 2013 overview

Details

Study type	**Non-randomised comparative study (retrospective)**
Country	The Netherlands
Recruitment period	1999–2002
Study population and number	Women with abnormal uterine bleeding and submucous myomas. **n=200 (28 hysteroscopic morcellation versus 172 transcervical resection using a resectoscope)**
Age and sex	Age range 20–72 years
Patient selection criteria	Pedunculated submucous myomas with no intramural extension (type 0) and sessile myomas with less than 50% intramural extension (type I). Patients with submucous myomas with more than 50% intramural extension (type II) were excluded.
Technique	All patients had diagnostic hysteroscopy. General or regional anaesthesia was used. Prototype of Intra Uterine Morcellator (IUM, Smith and Nephew Endoscopy, USA) was used. Preoperative, perioperative and postoperative management of all patients was identical except for the device and distension fluid used for tissue removal.
Follow-up	**3 months**
Conflict of interest/source of funding	Financial support was received from Smith and Nephew, USA.

Analysis

Study design issues: Results of earlier case series published by the same authors evaluating the transcervical resection of submucous myomas were used for comparison. Early in the series, electrolyte measurements were done in some patients with fluid deficit of more than 1000 ml saline. The study also reported separate results for patients with polyps but they have not been included here.

Study population issues: The authors reported that there were no obvious differences in baseline characteristics between the 2 groups.

Other issues: The authors note that further studies and improvements are planned.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **200 (28 versus 172)** The myomas were removed completely in a single procedure in 93% (26/28) of patients (in 2 patients with type I myomas, 'extensive pathology' [not otherwise described] meant the procedure was stopped before complete resection was achieved because of the risk of excessive fluid deficit; complete resection was obtained in a second procedure). **Mean operating time (minutes)** • Hysteroscopic morcellation=16.4 (95% CI 12.6 to 20.2) • Conventional resection=42.2 (95% CI 39.7 to 44.7) **Fluid loss deficit (ml)** • Hysteroscopic morcellation=660.0 (95% CI 418.6 to 901.4) • Conventional resection=741.8 (95% CI 645.9 to 837.7) In the hysteroscopic morcellation group, there were positive correlations between operating time and fluid deficit, between operating time and fluid used, and between fluid deficit and fluid used. Operating time and fluid deficit decreased over time, suggesting a learning curve effect. All patients were discharged within 24 hours. All patients were symptom free at the 3-month follow-up visit.	No evidence of fluid overload was seen. No abnormal electrolyte values were seen, and no obvious electrolyte changes were observed. No intraoperative or postoperative bleeding needing treatment occurred. All recoveries were uneventful.
Abbreviations used: CI, confidence interval	

Study 3 Hamerlynck TWO (2011) – included in 2013 overview

Details

Study type	**Case series (retrospective)**
Country	The Netherlands
Recruitment period	2006–9
Study population and number	Women with type 0, I or II myomas (mean myoma diameter=2 cm) **n=37**
Age and sex	Median age=45 years (range 26–49)
Patient selection criteria	Selection criteria not described. 62% (23/37) of patients had type 0 myoma, 30% (11/37) had type I myoma and 8% (3/37) of patients had a type II myoma.
Technique	Procedures were done under spinal or general anaesthesia. All patients received antibiotic prophylaxis. Morcellation was done with the TRUCLEAR hysteroscopic morcellator (Smith and Nephew, USA).
Follow-up	**Not reported**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Efficacy	**Safety**
Number of patients analysed: **37** Conversion to resectoscopy was necessary for the 3 patients with type II myomas. Mean operating time=18.2 minutes Median fluid deficit=440 ml (range 100–890) Pathology analysis confirmed the presence of a myoma in all cases.	The authors stated that there were no complications.

Study 4 Miller C (2009) – included in 2013 overview

Details

Study type	**Case series (retrospective)**
Country	USA
Recruitment period	2008–9
Study population and number	Premenopausal women with polyps, type 0, I or II myomas (mean myoma size=31.7 mm [range15–50]) **n=11 patients (14 polyps, 2 type 0 myomas, 3 type I myomas, 1 type II myoma)**
Age and sex	Median 41 years (range 29–58)
Patient selection criteria	Not described.
Technique	Procedures were done under general anaesthesia or intravenous sedation using a new hysteroscopic morcellator (Interlace Medical Inc., USA). Normal saline solution was used for distension and irrigation.
Follow-up	**Not reported**
Conflict of interest/source of funding	Study sponsored by Interlace Medical Inc.

Analysis

Study population issues: In this study, 70% (14/20) of the abnormalities in the 11 patients were polyps: 5 patients had multiple intrauterine pathologies, 5 had a single intrauterine myoma and 1 patient had a single polyp.

Key efficacy and safety findings

Efficacy	**Safety**
Number of patients analysed: **11** All patients were treated in a single session. Mean morcellation time for complete resection (data for myomas): • Type 0 myomas=2 minutes 19 seconds • Type I myomas=9 minutes 10 seconds Target pathology was 50% resected (100% of the intrauterine portion was removed) in the single patients with type II myoma (morcellation time=11 minutes 49 seconds). Tissue remaining in the uterine wall was removed by laparoscopic surgery. Mean fluid deficit (ml): • Type 0 myomas=205 (range 200–210) • Type I myomas=1300 (range 500–1900) (not recorded for type II myoma)	Authors reported that no patient experienced either an acute or delayed onset adverse event based on a review of medical records at 3 to 10 months after the procedure.

Study 5 Haber K (2014)

Details

Study type	**Review of Manufacturer and User Facility Device Experience (MAUDE) database**
Country	USA
Recruitment period	Database search=June 2014
Study population and number	**n=119 events** Women undergoing hysteroscopic surgery for the removal of intrauterine polyp or fibroid with a reciprocating morcellator.
Age and sex	not reported
Patient selection criteria	The database was searched for the following key words: 'Myosure', 'Truclear', 'hysteroscopic reciprocating morcellator', 'Interlace' and 'hysteroscope', 'Myosure' and 'hysteroscopy', 'Smith & Nephew' and 'hysteroscope'.
Technique	The Truclear™ hysteroscopic morcellator (Smith & Nephew, USA) and the Myosure® tissue removal system (Hologic, USA) were used.
Follow-up	**not reported**
Conflict of interest/source of funding	not reported

Analysis

Study design issues: Reports were reviewed individually for annotations of patient injury or death and were categorised by date reported, date of occurrence, type of morcellation device, type of complication, brief description and who reported the incident.

Study population issues:

- Women treated for polyps were also included.
- Each company was contacted to provide an estimate of the number of units sold to date in the USA as a surrogate of the number of procedures performed.
- Duplicate reports were identified and removed.

Key efficacy and safety findings

Safety

Adverse events reported on MAUDE database

Major complications	Truclear	Myosure	Total
Death	0	2	2
Bowel damage	3	9	12
Admission to intensive care unit	1	13	14
Hysterectomy	1	5	6
Unknown cause of admission	1	2	3
Total	**6**	**31**	**37**

Minor complications	Truclear	Myosure	Total
Uncomplicated fluid overload (resolved spontaneously or with intravenous Lasix)	1	18	19
Pelvic infection	0	4	4
Uterine perforation (needing no additional surgery or treatment)	6	22	28
Postoperative bleeding (controlled with non-invasive measures)	1	5	6
Device failure	9	16	25
Total	**17**	**65**	**82**

2 patients with bowel damage needed temporary colostomies and were admitted into the intensive care unit.

2 patients had a hysterectomy ‘per patient request’ after the diagnoses of uterine perforation and a failed endometrial ablation. 3 patients needed hysterectomy because of excessive blood loss.

11 patients with fluid overload needed intubation and admission to the intensive care unit.

Device failure included metal shavings and broken pieces of device visualised in the uterine cavity, poor visualisation, failure of outflow, and a defective device that would not activate. In 1 reported case, the blade fell into the uterine cavity and could not be retrieved. A hysterectomy was done and the patient did well postoperatively.

Of the 2 deaths, 1 was in a patient with multiple comorbidities such as chronic hypertension and obesity; the patient desaturated during anaesthesia and was diagnosed with pulmonary embolism and died. The second patient was an elderly woman who ‘was not well’; she was readmitted the day after her procedure and died shortly after. An exact cause of death was not reported.

It is estimated that approximately 80,000 Myosure devices have been sold since FDA approval in 2009 and an estimated 100,000 Truclear procedures have been done since 2004.

Estimated complication rate=0.07% (119/180,000); 0.1% for the Myosure hysteroscopic morcellator and 0.02% for the Truclear device.

Study 6 Rubino RJ (2014)

Details

Study type	**Randomised controlled trial (comparing an office setting against an ambulatory surgical centre)**
Country	USA
Recruitment period	Not reported
Study population and number	Pre or peri-menopausal women with submucosal myomas or polyps and abnormal uterine bleeding **n=74 patients (42 myomas, 66 polyps)**
Age and sex	Mean 41 years
Patient selection criteria	Intrauterine polyps or submucosal myomas which were compatible with office-based treated based on 1 or more of the following criteria: 1 or more polyps, with at least 1 of the polyps ≥1.5cm and ≤3.0cm diameter with a broad based attachment to the uterine wall; up to 2 type 0 or type 1 myomas with at least 1 of the myomas being ≥1.5cm and none of the myomas being >3.0cm; polyps plus up to 2 type 0 or type 1 myomas with at least 1 of the myomas being ≥1.5cm and ≤3.0cm and none of the myomas being >3.0cm. Exclusion criteria: known or suspected cancer; contraindication or allergy to local anaesthetic; history of chronic narcotic use; previous uterine artery embolisation; presence of intrauterine device at the time of the procedure; active pelvic inflammatory disease or pelvic/vaginal infection; type II submucosal myomas, fundal type I myomas, submucosal myomas >3.0cm or highly vascularised myomas.
Technique	All procedures were done using the Myosure® hysteroscopic tissue removal system (Hologic, USA).
Follow-up	**12 months**
Conflict of interest/source of funding	Study was sponsored by Hologic Inc.

Analysis

Study design issues: patients were randomised to receive the procedure either in an 'office' setting or in an ambulatory surgical centre. Different levels of analgesia were used in each setting. Each patient completed the Health Related Quality of Life (HRQOL) questionnaire and the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire prior to treatment and 12 months after treatment.

Study population issues: In this study, 61% (66/108) of the abnormalities in the 74 patients were polyps. Data are not presented separately for those women with myomas only.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **74**

Percentage pathology removal for myomas
- Overall=95.9%±6.8% (range 75%–100%)
- Office setting=94%±8.6% (range 75%–100%)
- Ambulatory surgical centre=99.8%±0.4% (range 99%–100%)

Proportion of myomas with 100% removal
- Overall=63.6%
- Office setting=52%
- Ambulatory surgical centre=83.3%

Mean resection time (seconds)
- Overall=143.0±293.3
- Office setting=189.3±376.9
- Ambulatory surgical centre=82.2±77.4

UFS-QOL symptom severity (higher scores indicate more severe symptoms) and HRQOL scores (higher scores indicate better quality of life)

	Overall	Office	surgical centre
UFS-QOL symptom score before procedure	67.5±15.4	68.3±16.3	66.4±14.0
UFS-QOL score at 12-months follow-up	22.3±22.6	39.1±24.7	38.2±21.1
UFS-QOL symptom severity improvement	45.2±23.2 p<0.01	42.7±24.0 p<0.01	48.3±21.6 p<0.01
HRQOL score before procedure	38.7±23.3	39.1±24.7	38.2±21.2
HRQOL score at 12-months follow-up	83.9±24.4	81.1±28.1	87.6±17.9
HRQOL improvement	45.5±25.1 p<0.01	42.3±25.3 p<0.01	49.4±24.3 p<0.01

Patient satisfaction (proportion of patients who reported that they were 'satisfied' or 'very satisfied'):
- Overall=89.2%
- Office setting=88.6%
- Ambulatory surgical centre=96.9%

Proportion of patients who would recommend treatment to other patients having similar symptoms:
- Overall=95.9%
- Office setting=95.5%
- Ambulatory surgical centre=100%

Safety

Adverse events=2.7% (2/74; 1 patient experienced pain that was considered to be mild and 1 patient had diarrhoea and food poisoning).

Abbreviations used: HRQOL, health related quality of life; UFS-QOL, uterine fibroid symptom and quality of life

Study 7 Rothenberg S (2014)

Details

Study type	**Case series (retrospective)**
Country	USA
Recruitment period	2006–12
Study population and number	Patients with benign endometrial disease **n=28 (55% polyps, 18% fibroids, 15% filling defect on sonohysterogram, 9% abnormal uterine bleeding, 3% uterine synechiae)**
Age and sex	Mean age=34 years
Patient selection criteria	Not reported
Technique	Morcellation was done with the Truclear® hysteroscopic morcellator (Smith & Nephew, USA).
Follow-up	**Not reported**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: Small, retrospective case series that included women with a variety of indications.

Study population issues: Only a small proportion of women (18%) were treated for uterine leiomyomas.

Key efficacy and safety findings

Efficacy	**Safety**
Number of patients analysed: **28** Mean operative time(minutes)=47±20.9 Mean fluid deficit (ml)=785±956.7	Overall complication rate=6% • Uterine perforation, n=1 (noted at the time of dilation and the intrauterine morcellator was not activated inside the morcellator) • Cervical injury, n=1 • Premature termination of the morcellator device, n=3 (1 because of inadequate distension, 2 because staff were unable to properly prime and initiate the fluid management system)

Efficacy

Operating time

A randomised controlled trial of 60 patients treated by hysteroscopic morcellation or conventional hysteroscopic resection reported mean operating times of 11 and 17 minutes respectively (p=0.008)[1]. A non-randomised comparative study of 200 patients treated by hysteroscopic morcellation or conventional hysteroscopic resection reported mean operating times of 16 minutes (95% confidence interval [CI] 13 to 20) and 42 minutes (95% CI 40 to 45) respectively[2]. A case series of 37 patients reported a mean operating time of 18 minutes[3].

Fluid deficit

The randomised controlled trial of 60 patients treated by hysteroscopic morcellation or conventional hysteroscopic resection reported mean fluid deficits (the amount of distending fluid infused during a procedure minus the amount of fluid recovered) of 409 and 545 ml respectively (p=0.224)[1]. The non-randomised comparative study of 200 patients treated by hysteroscopic morcellation or conventional hysteroscopic resection reported mean fluid deficits of 660 ml (95% CI 419 to 901) and 742 ml (95% CI 646 to 838) respectively[2]. The case series of 37 patients reported a median fluid deficit of 440 ml (range 100–890)[3].

Symptom relief

The non-randomised comparative study of 200 patients treated by hysteroscopic morcellation or conventional hysteroscopic resection reported that all patients were symptom free at the 3-month follow-up visit[2]. A randomised controlled trial of 74 patients with myomas or polyps treated by hysteroscopic morcellation in an office setting or an ambulatory surgical centre reported that symptom severity, measured using the uterine fibroid symptom-quality of life score, decreased from 67.5 at baseline to 22.3 at 12-months' follow-up (p<0.01)[6]. In the same study, health-related quality of life, measured using the health-related quality of life score, improved from 38.7 at baseline to 83.9 at 12-months' follow-up (p<0.01).

Safety

Bowel damage

Bowel damage was reported in 12 patients treated by hysteroscopic morcellation in a review of the Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database: 2 of these patients needed temporary colostomies and were admitted into the intensive care unit[5]. The review estimated that approximately 180,000 hysterosopic morcellation procedures had taken place during the study period.

Death

Death was reported in 2 patients treated by hysteroscopic morcellation in the review of the FDA MAUDE database[5]. One patient had multiple comorbidities such as chronic hypertension and obesity; the patient desaturated during anaesthesia and was diagnosed with pulmonary embolism and died. The second patient was an

elderly woman who 'was not well'; she was readmitted the day after her procedure and died shortly after. An exact cause of death was not reported.

High fluid deficit or fluid overload

Fluid overload that needed treating by intubation and admission to the intensive care unit was reported in 11 patients in the review of the FDA MAUDE database[5]. Uncomplicated fluid overload that resolved spontaneously or with conservative treatment was reported in 19 patients in the same review. In addition, hysteroscopic morcellation was aborted prematurely in 1 patient because of an imminent fluid overload in a randomised controlled trial of 60 patients treated by hysteroscopic morcellation or conventional hysteroscopic resection[1].

Hysterectomy

Hysterectomy was reported in 6 patients in the review of the FDA MAUDE database: 3 were because of excessive blood loss, 2 were at the patient's request after the diagnoses of uterine perforation and a failed endometrial ablation, and 1 was due to device failure (see below)[5].

Uterine perforation

Uterine perforation that needed no additional surgery or treatment was reported in 28 patients in the review of the FDA MAUDE database[5].

Pelvic infection

Pelvic infection was reported in 4 patients in the review of the FDA MAUDE database[5].

Postoperative bleeding

Postoperative bleeding that could be controlled with non-invasive measures was reported in 6 patients in the review of the FDA MAUDE database[5].

Device failure

Device failure, including metal shavings and broken pieces of device visualised in the uterine cavity, poor visualisation, failure of outflow, and a defective device that would not activate, was reported in 25 patients in the review of the FDA MAUDE database[5]. In 1 reported case, the blade fell into the uterine cavity and could not be retrieved. A hysterectomy was done and the patient did well postoperatively.

Other

Hospital admission due to an unknown cause was reported in 3 patients in the review of the FDA MAUDE database[5].

Validity and generalisability of the studies

- The randomised controlled trial included a high proportion of patients with polyps rather than fibroids; the results were not reported separately[1].

- Three of the published studies were from the Netherlands.
- The longest follow-up is 12 months, reported in 1 study[6].
- The review of events reported on the MAUDE database used the number of devices sold as a surrogate for the number of procedures done to calculate an approximate complication rate.
- Three studies excluded patients with type II myomas[1,2,6]. In 1 study 3 patients with type II myomas were included, all of whom needed conversion to conventional hysteroscopic resection[3]. In another study, the morcellator removed 50% of the target pathology in the single patient with a type II myoma[4].
- The randomised controlled trial included only submucous myomas smaller than 3 cm[1]. The mean myoma diameter in 1 case series was 2 cm[3].

Existing assessments of this procedure

A review of morcellation during uterine tissue extraction was published by AAGL – Advancing Minimally Invasive Gynecology Worldwide, in May 2014[8]. The review states that 'hysteroscopic morcellation differs from abdominal morcellation because it occurs within the uterus; however, in the absence of tubal ligation, tissue fragments could be introduced into the peritoneal cavity retrograde via the fallopian tubes…The risk of removing a uterine mesenchymal tumour during hysteroscopic morcellation of a presumed uterine myoma has not been quantified, but likely happens more rarely than when performing an abdominal procedure for presumed uterine myoma. Hysteroscopy remains an appropriate manner to remove symptomatic submucosal uterine myomas in premenopausal women and need not be exchanged for definitive treatment (i.e. hysterectomy) simply to avoid morcellation.'

The Royal College of Obstetricians and Gynaecologists and the British Society of Gynaecological Endoscopists published a joint guideline 'Best practice in outpatient hysteroscopy' in March 2011. This includes recommendations on service provision, analgesia, cervical preparation, type of hysteroscope, distension medium, local anaesthesia and cervical dilatation, sedation and vaginoscopy for outpatient hysteroscopy[9].

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Magnetic resonance image-guided transcutaneous focused ultrasound for uterine fibroids. NICE interventional procedure guidance 413 (2011). Available from www.nice.org.uk/guidance/IPG413

- Uterine artery embolisation for fibroids. NICE interventional procedure guidance 367 (2010). Available from www.nice.org.uk/guidance/IPG367
- Laparoscopic techniques for hysterectomy. NICE interventional procedure guidance 239 (2007). Available from www.nice.org.uk/guidance/IPG239
- Endometrial cryotherapy for menorrhagia. NICE interventional procedure guidance 157 (2006). Available from www.nice.org.uk/guidance/IPG157
- Photodynamic endometrial ablation. NICE interventional procedure guidance 47 (2004). Available from www.nice.org.uk/guidance/IPG47
- Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids. NICE interventional procedure guidance 30 (2003). Available from www.nice.org.uk/guidance/IPG30
- Laparoscopic laser myomectomy. NICE interventional procedure guidance 23 (2003). Available from www.nice.org.uk/guidance/IPG23

Guidelines

- Heavy menstrual bleeding. NICE guideline CG44 (2007). Available from www.nice.org.uk/guidance/CG44

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

T Justin Clark, Mary Connor, Sameer Umranikar (British Society for Gynaecological Endoscopy), Moiad Alazzam, Mary Ann Lumsden, Ertan Saridogan (Royal College of Obstetricians and Gynaecologists)

- Three specialist advisers have never performed the procedure and 3 have performed it at least once.
- Four specialist advisers consider the procedure to be definitely novel and of uncertain safety and efficacy; 2 consider it to be a minor variation on an existing procedure.
- Trans-cervical hysteroscopic myomectomy using a resectoscope is the comparator for this procedure.
- Theoretical adverse events: incomplete procedure, cervical trauma secondary to dilatation requiring a suture to be placed, lower abdominal cramps, morcellation of

malignant tissue, spreading endometrial cancer and upstaging, uterine perforation that may lead to injury of intra-abdominal organs such as bowel and bladder, fluid overload, haemorrhage and infection.

- Anecdotal adverse events: moderate vaginal bleeding that resolved spontaneously, blade detachment from machine.
- Adverse events reported in the literature: perforation of the uterus, bowel injury, haemorrhage, ongoing discharge, pain, infection, fluid overload and pulmonary oedema.
- Key efficacy outcomes are: proportion of fibroid removed by morcellator at first procedure, need for repeat procedures to remove fibroid remnants, relief of symptoms (reduction in menstrual blood loss, reduction or stopping of intermenstrual bleeding), need for further treatment or surgery to manage initial symptoms, reduction in incidence of miscarriage, duration of pregnancy and live birth rate.
- Fibroids with a significant intramural component are the most difficult to remove with any technique. The design of the morcellator limits its ability to reach the intramural portions, although this also reduces the risk of uterine perforation. Type 2 fibroids, where more than 50% is intramural and less than 50% within the uterine cavity may not be adequately treated by the morcellator, at least not with 1 procedure.
- One adviser noted that the safety and cancer risk dissemination is a current debate that should be addressed for hysteroscopic morcellator to establish safety.
- Five specialist advisers thought that the procedure would have a moderate impact on the NHS in terms of numbers of patients and use of resources; 1 adviser thought the impact would be minor.

Patient commentators' opinions

NICE's Public Involvement Programme sent 14 questionnaires to 1 NHS trust for distribution to patients who had the procedure (or their carers). NICE received 1 completed questionnaire.

The patient commentator's views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

The FDA (the US Food and Drug Administration) issued a US safety communication in April 2014 and an update in November 2014 that discourages the use of **laparoscopic** power morcellation during hysterectomy or myomectomy for the treatment of fibroids. The safety communication states: 'When used for hysterectomy or myomectomy in women with uterine fibroids, laparoscopic power morcellation poses a risk of spreading unsuspected cancerous tissue, notably uterine sarcomas, beyond the uterus. The FDA is warning against using laparoscopic power morcellators in the majority of women undergoing hysterectomy or myomectomy for uterine fibroids. Health care providers and patients should carefully consider available alternative treatment options for the removal of symptomatic uterine fibroids. The report made the following recommendations for healthcare providers:

- Be aware of the following new contraindications recommended by the FDA;

1. Laparoscopic power morcellators are contraindicated for removal of uterine tissue containing suspected fibroids in patients who are peri- or post-menopausal, or are candidates for en bloc tissue removal, for example through the vagina or mini-laparotomy incision. (Note: These groups of women represent the majority of women with fibroids who undergo hysterectomy and myomectomy.)

2. Laparoscopic power morcellators are contraindicated in gynaecologic surgery in which the tissue to be morcellated is known or suspected to contain malignancy.

- Be aware of the following new boxed warning recommended by the FDA:

The FDA warns that uterine tissue may contain unsuspected cancer. The use of laparoscopic power morcellators during fibroid surgery may spread cancer, and decrease the long-term survival of patients. This information should be shared with patients when considering surgery with the use of these devices.

- Carefully consider all the available treatment options for women with uterine fibroids.

- Thoroughly discuss the benefits and risks of all treatments with patients. Be certain to inform the small group of patients for whom laparoscopic power morcellation may be an acceptable therapeutic option that their fibroid(s) may contain unexpected cancerous tissue and that laparoscopic power morcellation may spread the cancer, significantly worsening their prognosis. This population might include some younger women who want to maintain their fertility or women not yet peri-menopausal who wish to keep their uterus after being informed of the risks.'

An Immediately In Effect (IIE) guidance document was issued at the same time ('Immediately in Effect Guidance Document: Product Labeling for Laparoscopic Power Morcellators. Guidance for Industry and Food and Drug Administration Staff') that asks manufacturers of new and existing **laparoscopic** power morcellators to include two contraindications and a boxed warning in their product labelling. In this document, it states that the guidance does not apply to hysteroscopic morcellators, which have a different principle of operation. 'FDA believes that, when used in accordance with current indications and instructions for use, hysteroscopic

morcellators do not pose the same risk as the devices addressed in this guidance because any sarcomatous tissue present does not enter the peritoneal cavity.'

Ongoing trial: The hysteroscopic morcellator versus the bipolar resectoscope for removal of lager intrauterine polyps, removal of submucous myomas and removal of residual placental tissue: a randomised controlled trial (NCT01537822). Belgium and the Netherlands; Estimated enrolment=222; Study start date May 2011; Estimated study completion date September 2014.

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Appendix A: Additional papers on hysteroscopic morcellation of uterine leiomyomas (fibroids)

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Cohen S, Greenberg JA. (2011) Hysteroscopic morcellation for treating intrauterine pathology. Reviews in Obstetrics and Gynecology 4: 73–80	Review	Hysteroscopic morcellation allows for the use of smaller diameter hysteroscopes that need less cervical dilation and less anaesthesia than traditional hysteroscopic resection.	No meta-analysis. All the published studies cited are included in table 2.
Pakrashi T, Ressler IB, Sroga JM et al. (2013) Hysteroscopic enucleation of type II submucosal uterine leiomyomas using a TRUCLEAR hysteroscopic morcellator: case report and review of the literature. Journal of Laparoendoscopic & Advanced Surgical Techniques 23: 378-382	n=1	Case report - complete enucleation of a Type II leiomyoma Hysteroscopic uterine leiomyoma enucleation should only be performed in experienced hands. Inadvertent enucleation of a Type II leiomyoma with a THM device is described, with review of key surgical principles that guided safe resection.	Case report – no safety events identified

Appendix B: Related NICE guidance for hysteroscopic morcellation of uterine leiomyomas (fibroids)

Guidance	Recommendations
Interventional procedures	**Magnetic resonance image-guided transcutaneous focused ultrasound for uterine fibroids. NICE interventional procedure guidance 413 (2011).** 1.1 Current evidence on the efficacy of magnetic resonance image (MRI)-guided transcutaneous focused ultrasound for uterine fibroids in the short term is adequate, although further treatment may be required and the effect on subsequent pregnancy is uncertain. There are well-recognised complications but the evidence on safety is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance and audit. 1.2 During the consent process clinicians should inform patients that their symptoms may not be relieved, that their symptoms may return, and that further procedures may therefore be required. They should also inform patients about the risk of skin burns. Patients contemplating pregnancy should be informed that the effects of the procedure on fertility and on pregnancy are uncertain. 1.3 Patient selection should be carried out by a multidisciplinary team including a gynaecologist and an appropriate imaging specialist. 1.4 The procedure should only be carried out by clinicians with specific training in this technique. 1.5 NICE encourages further research into the efficacy of MRI-guided transcutaneous focused ultrasound for uterine fibroids. Research studies should report long-term outcomes, including the need for further treatment. Data on the incidence and outcomes of subsequent pregnancy in patients who choose this procedure because they wish to maintain or improve their fertility are particularly important. **Uterine artery embolisation for fibroids. NICE interventional procedure guidance 367 (2010).** 1.1 Current evidence on uterine artery embolisation (UAE) for fibroids shows that the procedure is efficacious for symptom relief in the short and medium term for a substantial proportion of patients. There are no major safety concerns. Therefore this procedure may be used provided that normal arrangements are in place for clinical governance and audit. 1.2 During the consent process patients should be informed, in particular, that symptom relief may not be achieved in some women, that symptoms may return and that further procedures may therefore

	be required. Patients contemplating pregnancy should be informed that the effects of the procedure on fertility and on pregnancy are uncertain. 1.3 Patient selection should be carried out by a multidisciplinary team, including a gynaecologist and an interventional radiologist. 1.4 NICE encourages further research into the effects of UAE compared with other procedures to treat fibroids, particularly for women wishing to maintain or improve their fertility. **Laparoscopic techniques for hysterectomy. NICE interventional procedure guidance 239 (2007).** 1.1 Current evidence on the safety and efficacy of laparoscopic techniques for hysterectomy (including laparoscopically-assisted vaginal hysterectomy [LAVH], laparoscopic hysterectomy [LH], laparoscopic supracervical hysterectomy [LSH] and total laparoscopic hysterectomy [TLH]) appears adequate to support their use, provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians should advise women that there is a higher risk of urinary tract injury and of severe bleeding associated with these procedures, in comparison with open surgery. 1.3 Advanced laparoscopic skills are required for these procedures, and clinicians should undergo special training and mentorship. The Royal College of Obstetricians and Gynaecologists has developed an Advanced Training Skills Module, 'Benign Gynaecological Surgery: Laparoscopy'. This would need to be supplemented by further training in order to achieve the skills required for total laparoscopic hysterectomy. **Endometrial cryotherapy for menorrhagia. NICE interventional procedure guidance 157 (2006).** 1.1 Limited short-term evidence on the safety and efficacy of endometrial cryotherapy for menorrhagia appears adequate to support the use of this procedure in carefully selected patients provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians should ensure that patients understand that there are alternative treatment options with different likelihoods of achieving complete amenorrhea or normal periods. Appropriate patient selection and patient choice are both important. In addition, use of the Institute's information for the public is recommended. **Photodynamic endometrial ablation. NICE interventional procedure guidance 47 (2004).** 1.1 Current evidence on the safety and efficacy of photodynamic

	endometrial ablation does not appear adequate to support the use of this procedure outside formal research. It is suitable for use only within good quality research studies approved by a research ethics committee and with explicit patient consent. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. The Institute is not undertaking further investigation at present. **Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids. NICE interventional procedure guidance 30 (2003).** 1.1 Evidence on safety and efficacy outcomes of MR image-guided percutaneous laser ablation of uterine fibroids is insufficient to support its use without special arrangements for consent and for audit or research. Clinicians wishing to undertake MR image-guided percutaneous laser ablation should inform the clinical governance leads in their Trusts. They should ensure that women offered the procedure understand the uncertainty about its safety and efficacy and should provide them with clear written information. Use of the Institute's information for the public is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking further investigation at present. **Laparoscopic laser myomectomy. NICE interventional procedure guidance 23 (2003).** 1.1 Current evidence on the safety and efficacy of laparoscopic laser myomectomy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. Clinicians wishing to undertake laparoscopic laser myomectomy should inform the clinical governance leads in their Trusts. They should ensure that patients offered it understand the uncertainty about the procedure's safety and efficacy and should provide them with clear written information. Use of the Institute's information for the public is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking further investigation at present. 1.2 Clinicians undertaking this procedure should undergo training as recommended by the Royal College of Obstetricians and Gynaecologists Working Party on Training in Endoscopic Surgery.
Clinical guidelines	**Heavy menstrual bleeding. NICE guideline CG44 (2007).** **1.7 Further interventions for uterine fibroids associated with heavy menstrual bleeding** 1.7.1 For women with large fibroids and HMB, and other significant symptoms such as dysmenorrhoea or pressure symptoms, referral for consideration of surgery or uterine artery embolisation (UAE) as first-

	line treatment can be recommended. 1.7.2 UAE, myomectomy or hysterectomy should be considered in cases of HMB where large fibroids (greater than 3 cm in diameter) are present and bleeding is having a severe impact on a woman's quality of life. 1.7.3 When surgery for fibroid-related HMB is felt necessary then UAE, myomectomy and hysterectomy must all be considered, discussed and documented. 1.7.4 Women should be informed that UAE or myomectomy may potentially allow them to retain their fertility. 1.7.5 Myomectomy is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus. 1.7.6 UAE is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus and/or avoid surgery. 1.7.7 Prior to scheduling of UAE or myomectomy, the uterus and fibroid(s) should be assessed by ultrasound. If further information about fibroid position, size, number and vascularity is required, MRI should be considered. 1.7.8 Pretreatment before hysterectomy and myomectomy with a gonadotrophin-releasing hormone analogue for 3 to 4 months should be considered where uterine fibroids are causing an enlarged or distorted uterus. 1.7.9 If a woman is being treated with gonadotrophin-releasing hormone analogue and UAE is then planned, the gonadotrophin-releasing hormone analogue should be stopped as soon as UAE has been scheduled.

Appendix C: Literature search for hysteroscopic morcellation of uterine leiomyomas (fibroids)

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	03/11/2014	Issue 10 of 12, October 2014
Database of Abstracts of Reviews of Effects – DARE (Cochrane Library)	03/11/2014	Issue 4 of 4, October 2014
HTA database (Cochrane Library)	03/11/2014	Issue 4 of 4, October 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	03/11/2014	Issue 10 of 12, October 2014
MEDLINE (Ovid)	03/11/2014	1946 to October Week 4 2014
MEDLINE In-Process (Ovid)	03/11/2014	October 30, 2014
EMBASE (Ovid)	03/11/2014	1974 to 2014 Week 44
CINAHL (NLH Search 2.0)	03/11/2014	n/a
PubMed	03/11/2014	n/a
JournalTOCS	03/11/2014	n/a

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Uterine Neoplasms/ and Leiomyoma/
2	(uter* adj3 (neoplasm* or tumour* or tumor* or growth* or fibroma* or leiomyoma* or leimyoma* or angioleiomyoma* or angiomyoma* or myofibroma* or leyomyoma)).tw.
3	(fibromyoma* or fibroleiomyoma).tw.
4	((fibroid* or myoma*) adj3 (tumour* or tumor* or uter* or submucos* subseros* or intramural* or pedunculated or cervical)).tw.
5	or/1-4
6	(hysteroscop* adj5 (morcellat* or cut* or suck* or suction* or remov* or myomectom* or excis*)).tw.
7	Hysteroscopy/ and uterine myomectomy/
8	(transcervical adj3 resection).tw.
9	TCRE.tw.
10	Myosure.tw.
11	Truclear.tw.
12	or/6-11
13	5 and 12
14	limit 13 to ed=20140624-20140831