Embosphere®

Microspheres

CAUTION: Federal (U.S.A.) law restricts this device to use by or on the order of a licensed physician.

INTENDED USE:
Embosphere Microspheres are indicated for use in embolization of arteriovenous malformations, hypervascular tumors, and symptomatic uterine fibroids.

CLINICAL APPLICATIONS FOR UTERINE FIBROIDS:
Uterine fibroid embolization (UFE) is an alternative treatment for women requiring treatment for relief of symptoms attributed to uterine fibroids including heavy menstrual bleeding, pelvic pain or pressure, and/or urinary dysfunction.

MAGNETIC RESONANCE IMAGING:
Embosphere Microspheres are made of tris-acryl polymer impregnated with porcine gelatin and have no ferrous composition.

DEVICE DESCRIPTION:
Embosphere Microspheres are part of a family of embolic materials based on Merit Medical's proprietary microsphere technology. These spheres are designed to offer controlled, targeted embolization.

Embosphere Microspheres are biocompatible, hydrophilic, nonresorbable, microspheres produced from an acrylic polymer and impregnated with porcine gelatin. Embosphere Microspheres are available in a range of calibrated sphere sizes.

DEVICE PACKAGING:
- Embosphere Microspheres are contained in a sterile, 20 mL pre-filled syringe, packaged in a peel-away pouch.
- Each syringe contains approximately 1.0 mL or 2.0 mL of Embosphere Microspheres in a pyrogen-free, sterile, physiological saline.

The following contraindications, warnings, precautions, and instructions for use are organized to present information applicable to all indications (i.e., hypervascular tumors, arteriovenous malformations and uterine fibroids) first, followed by indication-specific information (i.e., UFE and neurological).

CONTRAINDICATIONS:
All indications
- Patients intolerant to occlusion procedures
- Vascular anatomy or blood flow that precludes catheter placement or embolic agent injection
- Presence or likely onset of vasospasm
- Presence or likely onset of hemorrhage
- Presence of severe atheromatous disease
- Presence of feeding arteries smaller than distal branches from which they emerge
- Presence of arteries supplying the lesion not large enough to accept Embosphere Microspheres
- Presence of collateral vessel pathways potentially endangering normal territories during embolization
- Vascular resistance peripheral to the feeding arteries precluding passage of Embosphere Microspheres into the lesion
- In large diameter arteriovenous shunts (i.e., where the blood does not pass through an arterial/capillary/venous transition but directly from an artery to a vein)
- In the pulmonary vasculature

UFE Specific Contraindications
- Pregnant women
- Suspected pelvic inflammatory disease or any other active pelvic infection
- Any malignancy of the pelvic region
- Endometrial neoplasia or hyperplasia
- Presence of one or more submucosal fibroid(s) with more than 50% growth into the uterine cavity
- Presence of pedunculated serosal fibroid as the dominant fibroid(s)
- Fibroids with significant collateral feeding by vessels other than the uterine arteries

Neurological Specific Contraindications
- Presence of patent extra-to-intracranial anastomoses or shunts
- Presence of end arteries leading directly to cranial nerves
- In any vasculature where Embosphere Microspheres could pass directly into the internal carotid artery, vertebral artery, intracranial vasculature or the above listed vessels

WARNINGS:

All Indications
- Embosphere Microspheres contain gelatin of porcine origin, and therefore, could cause an immune reaction in patients who are hypersensitive to collagen or gelatin. Careful consideration should be given prior to using this product in patients who are suspected to be allergic to injections containing gelatin stabilizers.
- Studies have shown that Embosphere Microspheres do not form aggregates, and, as a result, penetrate deeper into the vasculature as compared to similarly sized PVA particles. Care must be taken to choose larger sized Embosphere Microspheres when embolizing arteriovenous malformations with large shunts to avoid passage of the spheres into the pulmonary or coronary circulation.
- Some of the Embosphere Microspheres may be slightly outside of the range, so the physician should be sure to carefully select the size of Embosphere Microspheres according to the size of the target vessels at the desired level of occlusion in the vasculature and after consideration of the arteriovenous angiographic appearance. The size of Embosphere Microspheres should be selected to prevent passage from artery to vein.
- Because of the significant complications of misembolization, extreme caution should be used for any procedures involving the extracranial circulation encompassing the head and neck, and the physician should carefully weigh the potential benefits of using embolization against the risks and potential complications of the procedure. These complications can include blindness, hearing loss, loss of smell, paralysis and death.
- Serious radiation-induced skin injury may occur to the patient due to long periods of fluoroscopic exposure, large patient diameter, angled x-ray projections, and multiple image recording runs or radiographs. Refer to your facility's clinical protocol to ensure the proper radiation dose is applied for each specific type of procedure performed. Physicians should monitor patients that may be at risk.
- Onset of radiation-induced injury to the patient may be delayed. Patients should be counseled on potential radiation side effects and whom they should contact if they show symptoms.
- Pay careful attention for signs of mistargeted embolization. During injection carefully monitor patient vital signs to include SaO_2 (e.g. hypoxia, CNS changes). Consider terminating the procedure, investigating for possible shunting, or increasing microsphere size if any signs of mistargeting occur or patient symptoms develop.
- Consider upsizing the microspheres if angiographic evidence of embolization does not quickly appear evident during injection of the microspheres.

UFE Specific Warnings

Warnings about UFE and Pregnancy
- The effects of UFE on the ability to become pregnant and carry a fetus to term, and on the development of the fetus, have not been determined. Therefore, this procedure should only be performed on women who do not intend future pregnancy.
- Women who become pregnant following UFE may be at increased risk for postpartum hemorrhage, preterm delivery, cesarean delivery, and malpresentation.
- Devascularization of the uterine myometrium resulting from UFE may theoretically put women who become pregnant following UFE at increased risk of uterine rupture.

Other UFE Warnings
- When using Embosphere Microspheres for uterine fibroid embolization, do not use microspheres smaller than 500 microns.
- An appropriate gynecologic work-up should be performed on all patients presenting for embolization of uterine fibroids (e.g., gynecologic history, fibroid imaging, endometrial sampling to rule out carcinoma in patients with abnormal menstrual bleeding).
- The diagnosis of uterine sarcoma could be delayed by taking a non-surgical approach (such as UFE) to treating fibroids. It is important to pay close attention to warning signs for sarcoma (e.g., rapid tumor growth, postmenopausal with new uterine enlargement, MRI findings) and to conduct a more thorough work-up of such patients prior to recommending UFE. Recurrent or continued tumor growth following UFE should be considered a potential warning sign for sarcoma and surgery should be considered.

Warnings about use of small microspheres
- Careful consideration should be given whenever use is contemplated of embolic agents that are smaller in diameter than the resolution capability of your imaging equipment. The presence of arteriovenous anastomoses, branch vessels leading away from the target area or emergent vessels not evident prior to embolization can lead to mistargeted embolization and severe complications.
- Microspheres smaller than 100 microns will generally migrate distal to anastomotic feeders and therefore are more likely to terminate circulation to distal tissue. Greater potential of ischemic injury results from use of smaller sized microspheres and consideration must be given to the consequence of this injury prior to embolization. The potential consequences include, swelling, necrosis, paralysis, abscess and/or stronger post embolization syndrome.
- Post embolization swelling may result in ischemia to tissue adjacent to target area. Care must be given to avoid ischemia intolerant, nontargeted tissue such as nervous tissue.

PRECAUTIONS:
All Indications
- Patients with known allergy to contrast medium may require corticosteroids prior to embolization.
- Additional evaluations or precautions may be necessary in managing periprocedural care for patients with the following conditions:
  - Bleeding diathesis or hypercoagulative state
  - Immunocompromise
- Do not use if the syringe, plunger seal, or tray package appear damaged.
- For single patient use only - contents supplied sterile - never reuse, reprocess, or resterilize the contents of a syringe that has been opened. Reusing, reprocessing or resterilizing may compromise the structural integrity of the device and or lead to device failure, which in turn may result in patient injury, illness or death. Reusing, reprocessing or resterilizing may also create a risk of contamination of the device and or cause patient infection or cross infection including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. All procedures must be performed according to accepted aseptic technique.
- Do not connect the 20 mL syringe with Embosphere Microspheres directly to a microcatheter for embolic delivery, as a catheter occlusion may result.
- The syringe is intended for embolic use only. Do not use for any other application.
- Select the size and quantity of Embosphere Microspheres appropriate for the pathology to be treated.
- Embolization with Embosphere Microspheres should only be performed by physicians who have received appropriate interventional embolization training in the region to be treated.

UFE Specific Precautions
- There is an increased chance of retro-migration of Embosphere Microspheres into unintended blood vessels as uterine artery flow diminishes. Embolization should be stopped when the vasculature surrounding the fibroid can no longer be visualized but before complete stasis in the uterine artery.
- UFE should only be performed by Interventional Radiologists who have received appropriate training for treatment of uterine leiomyomata (fibroids).

POTENTIAL COMPLICATIONS:
All Indications
Vascular embolization is a high-risk procedure. Complications may occur at any time during or after the procedure, and may include, but are not limited to, the following:
- Paralysis resulting from untargeted embolization or ischemic injury from adjacent tissue edema
- Undesirable reflux or passage of Embosphere Microspheres into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds, such as the internal carotid artery, pulmonary, or coronary circulations
- Pulmonary embolism due to arterial venous shunting
- Ischemia at an undesirable location, including ischemic stroke, ischemic infarction (including myocardial infarction), and tissue necrosis
- Capillary bed occlusion and tissue damage
- Vessel or lesion rupture and hemorrhage
- Vasospasm
- Recanalization
- Foreign body reactions necessitating medical intervention
- Infection necessitating medical intervention
- Complications related to catheterization (e.g., hematoma at the site of entry, clot formation at the tip of the catheter and subsequent dislodgment, and nerve and/or circulatory injuries, which may result in leg injury)
- Allergic reaction to medications (e.g., analgesics)
- Allergic reaction to contrast media or embolic material
- Pain and/or rash, possibly delayed from the time of embolization
- Death
- Blindness, hearing loss, loss of smell, and/or paralysis
- Additional information is found in the Warnings section

UFE Specific Potential Complications
- The most frequently anticipated post procedure complications are abdominal pain, discomfort, fever and/or nausea, collectively known as "Post-embolization Syndrome." Some patients may also experience constipation. This is generally managed with prescription or over-the-counter medications.
- Premature ovarian failure (i.e., menopause)
- Amenorrhea
- Infection of the pelvic region
- Uterine/ovarian necrosis
- Phlebitis
- Deep vein thrombosis with or without pulmonary embolism
- Vaginal discharge
- Tissue passage, fibroid sloughing, or fibroid expulsion post UFE
- Post-UFE intervention to remove necrotic fibroid tissue
- Vagal reaction
- Transient hypertensive episode
- Hysterectomy

Neurological Specific Potential Complications
- Ischemic stroke or ischemic infarction
- Neurological deficits, including cranial nerve palsies

STORAGE AND STERILITY:
- Embosphere Microspheres must be stored in a cool, dry and dark place in their original syringe and packaging.
- Use by the date indicated on the syringe label.
- Do not freeze.
- Do not resterilize.

INSTRUCTIONS FOR USE:
Inspect packaging prior to use to ensure seal integrity for maintenance of sterility.

- Carefully evaluate the vascular network associated with the lesion using high resolution imaging prior to beginning the embolization procedure.

- Embosphere Microspheres are available in a range of sizes. Because of the potential for misembolization and the inherent variability in sphere sizes, the physician should be sure to carefully select the size of Embosphere Microspheres according to the size of the target vessels at the desired level of occlusion in the vasculature.
- When embolizing arteriovenous malformations (AVMs), choose an Embosphere Microsphere size that will occlude the nidus without passing through the AVM.
- When embolizing uterine fibroids, choose an Embosphere Microsphere size of 500 microns or greater.
- Choose a delivery catheter based on the size of the target vessel and the microsphere size being used. Embosphere Microspheres can tolerate temporary compression of up to 33% in order to facilitate passage through the delivery catheter.
- Introduce the delivery catheter into the target vessel according to standard techniques. Position the catheter tip as close as possible to the treatment site to avoid inadvertent occlusion of normal vessels.
- Embosphere Microspheres are not radiopaque. It is recommended that the embolization be monitored using fluoroscopic visualization by adding the appropriate amount of contrast medium to the physiologic suspension fluid.

To deliver Embosphere Microspheres:
- Match the total volume in the syringe with the same volume of undiluted contrast, which will result in a 50% microsphere/saline and 50% contrast solution. Remove all air from the syringe. To evenly suspend the Embosphere Microsphere/contrast solution, gently invert the 20 mL syringe several times. Attach the 20 mL syringe to one port of the luer-lock 3-way stopcock. Attach a 1 mL or 3 mL injection syringe to another port on the stopcock and, if desired, a delivery catheter may be attached to the remaining port on the stopcock. Wait several minutes to allow the Embosphere Microspheres to suspend in the solution. Draw the Embosphere Microspheres/contrast solution into the injection syringe slowly and gently to minimize the potential of introducing air into the system. Purge all air from the system prior to injection. Inject the Embosphere Microspheres/contrast solution under flouroscopic visualization with the injection syringe using a slow pulsatile injection while observing the contrast flow rate. If there is no effect on the flow rate, repeat the delivery process with additional injections of the Embosphere Microspheres/contrast solution. Consider using larger sized Embosphere Microspheres if the initial injections do not alter the contrast flow rate. If the Embosphere Microspheres/contrast solution requires re-suspension, gently invert the 20 mL syringe several times. Exercise conservative judgment in determining the embolization endpoint.
- Femoral puncture can result in arterial spasm. This may predispose to femoral thrombosis (e.g., leg injury). Femoral patency should be re-assessed prior to final catheter removal.
- Upon completion of the treatment, remove the catheter while maintaining gentle suction so as not to dislodge Embosphere Microspheres still within the catheter lumen.
- Apply pressure to the puncture site until hemostasis is complete.
- Discard any open, unused Embosphere Microspheres.

Additional UFE specific instructions:
- At the discretion of the physician, pneumatic compression devices may be used for patients currently taking hormone therapy, uterine volume >1000cc, and patients that are overweight to lower the risk of deep vein thrombosis.
- Embolization should be stopped when the vasculature surrounding the fibroid can no longer be visualized but before complete stasis in the uterine artery. There is an increased chance of retro-migration of Embosphere Microsphere into unintended blood vessels as uterine artery flow diminishes.

UFE PATIENT COUNSELING INFORMATION:
- Patients should have a clear understanding prior to embolization of who will provide their post procedure care and whom to contact in case of an emergency after embolization. Patient information brochures are available and distributed by Merit Medical.
- UFE candidates should have an understanding of the potential benefits, risks, and adverse events associated with UFE. In particular, patients should understand that there is a chance their fibroid-related symptoms will not improve following UFE.

UFE CLINICAL STUDY SUMMARY:
Study Design

A prospective multi-center trial was conducted to study UFE using Embosphere Microspheres for treatment of symptomatic uterine fibroids. A total of 132 women who desired to keep their uterus and avoid surgery were treated by UFE in the study; 30 in an initial feasibility study and 102 in the pivotal study. Those patients included in the pivotal study were followed for 3 years, with clinical measures of outcome obtained at 3, 6, 12, 24 and 36 months after treatment. Seven investigational sites participated in the study.

The study was designed to determine whether UFE using Embosphere Microspheres could reduce symptoms associated with symptomatic fibroids, such as abnormal bleeding, pain, discomfort, and urinary problems.

Primary study endpoints included:

- Reduction in menstrual bleeding from baseline to 6 months post-UFE as measured using a Pictorial Bleeding Assessment Chart (PBLAC)
- Improvement in bulk symptoms (pelvic pain, pelvic discomfort/bloating, and urinary dysfunction) as measured using a patient symptom questionnaire
- Improvement in quality of life as measured using the SF-12 Health Status Questionnaire

Secondary endpoints included:

- Other measures of changes in menstrual bleeding
- Reduction of uterus and fibroid size
- Hospitalization time
- Time to return to normal activities
- Evaluations of patient satisfaction with the procedure

Adverse events and complications were also evaluated with respect to type, rate, and severity.

Eligibility criteria included age between 30 and 50 years, inclusive, infertile or no plans to become pregnant, one or more symptomatic uterine fibroids, uterine volume 250 cc or fibroid volume 4 cc, and baseline PBLAC ≥ 150. Women were excluded from the study if they were pregnant, had a history of pelvic inflammatory disease, submucosal fibroid(s) with more than 50% growth into the uterine cavity, pedunculated subserosal fibroid(s) as the dominant fibroid(s), significant collateral feeding by vessels other than uterine artery, adenomyosis as the dominant cause of symptoms, endometrial or pre-malignant hyperplasia, any malignancy of the pelvic region, any active infection of the pelvic region, known allergy to IV contrast or gelatin, bleeding diathesis, immunocompromised, post-menopausal or baseline FSH > 40 mIU/mL, or treatment with GnRH agonist within the previous 3 months.

Pre-treatment evaluations included routine gynecological exam and testing, standard laboratory testing, ultrasound or MRI, menstrual bleeding record (UFE group), and self-assessment questionnaires relating to overall health (SF-12), menstrual bleeding, and fibroid symptoms.

Study Results
Of the 102 patients enrolled in the pivotal study, 96 patients had complete baseline data and of these, 69 (72%) had known outcomes after 3 years after UFE treatment. Not all patients provided all outcome measures at the final follow-up interval, and the numbers providing follow-up are detailed in each of the tables provided.

Procedure, Discharge, and Recovery Information

All UFE procedures performed in both the feasibility and pivotal studies were technically successful with no intraoperative complications that prevented completion of the procedure. The majority (77%) of the UFE procedures were performed using a 5 Fr catheter with either a 4 Fr (19%) or 3 Fr (3%) in the remainder. Seventy-two patients were treated with 500-700 micron spheres, 66 patients with 700-900 micron spheres and 18 patients with 900-1200 micron spheres. Many of the patients were treated with more than one sphere size. The most common treatment approach was to start with a smaller sphere size and then to increase the size if necessary. The volume of spheres required varied inversely with the sphere size as an average of 7.2 cc of 500-700 micron spheres was used as compared to 6 cc of 700-900 micron spheres and 4.1 cc of 900-1200 micron spheres.

The majority of UFE patients underwent the procedure while under conscious sedation with a local anesthetic given at the puncture site. No UFE procedures were performed under general anesthesia. The average UFE procedure time from first arterial puncture to final catheter removal was 58 ± 28 minutes (range 10-140 minutes). Eighty-seven percent of the UFE patients were discharged from the hospital on the day following the embolization procedure and 12% on the same day as the procedure. UFE patients were back to work or returned to normal daily activities in an average of 10.7 days.

Primary Efficacy Endpoints

Menstrual Bleeding

To be eligible for UFE in the feasibility and pivotal studies, patients were required to have abnormally heavy menstrual bleeding, with a baseline score of ≥150 on the Pictorial Bleeding Assessment Chart (PBLAC) of Janssen et al. (1995). Additional measures were also used to assess changes in menstrual bleeding, including patient self-assessment of their bleeding level and a menorrhagia questionnaire. Changes in menstrual bleeding generally occurred quickly following UFE, with 92% of the patients showing improvement by 3 months. Out of the 102 patients from the pivotal study, only 48 patients completed the menorrhagia questionnaire at 36 months, and paired data were available from only 41 patients However, the results show a substantial and statistically significant improvement in scores (with lower scores being better) and the mean scores remained improved for the duration of the study (Table 1). These findings are well aligned with the patient self-assessment of menstrual bleeding (Table 2). At baseline, 54% of patients rated their bleeding as extremely heavy and 42% rated their bleeding as moderately heavy. During the 36-month follow-up, only 3% or less rated their bleeding as extremely heavy and less than 28% of patients complained of moderately heavy bleeding. At 36 months after treatment, 22% of patients noted that they were not having menstrual periods.

Table 1 – Results of the Menorrhagia Questionnaire

		All data		Paired data (n =41)*	
		Mean score standard deviation	Range	Mean score standard deviation	Range
Before Treatment (n =96)		47.9±13.1	14.29–83.33	45.2±13.5	14.3–83.3
After Treatment	3 mo (n =83)	24.5±13.1	7.1–64.3	22.9±10.7	7.1–54.8
	6 mo (n =83)	21.03±11.9	7.1–64.3	18± 8.6	7.1–52.4
	12 mo (n =78)	17.1±10.1	2.4–61.9	18.6±11.7	2.4–61.9
	24 mo (n =67)	19.7±11.8	0–54.8	17.8±9.4	0–54.8
	36 mo (n= 48)	19.2±11	0–57.1	20.1± 10.7	0–57.1

Note.—The difference between the scores at each time interval and that at baseline were statistically significant (P <.001). P value was calculated with tests, paired tests, and sign tests. * Paired data are from those patients who had data available at each follow-up interval (N 41).

Table 2 – Patient Assessment of Menstrual Bleeding

		Description of Bleeding				
		Extremely heavy	Moderately heavy	Normal	Light	No Periods
Before Treatment (n =95)		54 (57)	40 (42)	1 (1)	0 (0)	0 (0)
After Treatment	3 mo (n =87)	3 (3)	38 (44)	27 (31)	13 (15)	6 (7)
	6 mo (n =88)	3 (3)	25 (28)	37 (42)	18 (20)	5 (6)
	12 mo (n =83)	1 (1)	17 (20)	38 (46)	21 (25)	6 (7)
	24 mo (n =71)	2 (3)	17 (24)	33 (46)	15 (21)	4 (6)
	36 mo (n=59)	1 (2)	14 (24)	27 (37)	9 (15)	13 (22)

Note.—Data are given as numbers of patients. Numbers in parentheses are percentages.

Bulk Symptoms

Bulk symptoms of pain, discomfort and urinary problems (Table 3) were substantially improved in most patients, although a smaller number of patients had substantially improved urinary symptoms at each of the data intervals.

Table 3 – Bulk Symptom Status: Proportion of Patients with Moderate to Substantial Improvement after Embolization

	Symptom		
	Pelvic pain	Pelvic discomfort	Urinary problems
3 mo (n =86)	63 (73)	61 (71)	46 (53)
6 mo (n =87)	68 (78)	71 (82)	58 (66)
12 mo (n =81)	77 (83)	67 (81)	56 (69)
24 mo (n =73)	60 (83)	61 (83)	44 (62)
36 mo (n =59)	49 (83)	49 (83)	42 (69)

Note.—Data are given as numbers of patients. Numbers in parentheses are percentages.

Quality of Life

The SF-12 Health Status questionnaire was used to assess changes in general physical and mental health status following treatment. The goal of this endpoint was to demonstrate at least a moderate improvement in the overall quality of life. Results of the SF-12 Health Status questionnaire are presented in Table 4. This 12-question questionnaire is scored and normalized to a mean score of 50 and a standard deviation of 10 for the general U.S. population. The mean physical and mental summary score for patients before embolization was 45. The physical summary score increased to 51.8 by 3 months and to 53.7 by 36 months, whereas the mean mental score was 52.1 at 3 months and 53.3 at 36 months. The patient's perception of health status correspondingly increased, from a mean of 69.5 to 86.3 by 36 months. At the conclusion of the study, 84% of patients were very or moderately satisfied with the symptom control of the procedure.

Table 4 – Results of SF-12 Questionnaire with Regard to Overall Health Status and Satisfaction with Outcome

		Parameter Evaluated								
		Physical status			Mental status			Overall health status		No. of patients who were moderately or very satisfied
		Mean score standard deviation	Range	P value	Mean score standard deviation	Range	P value	Mean score standard deviation	Range	
Before Treatment (n =96)		45±8.3	26–61.6		45±11.5	22.3–63.4		69.5±19.1	0–100	
After Treatment	3 mo (n =88)	51.8±6.7	22.3–58.5	<.001	52.1±7.7	23.8–61.6	<.001	82.6±14.2	28.7–100	78 (89%)
	6 mo (n =88)	52.4±6.2	23.3–62.6	<.001	52.9 ±7.9	20.5–60.8	<.001	85.1±11.3	43.8–100	78 (89%)
	12 mo (n =82)	53.6±5.9	23.1–64.1	<.001	52.6±7.8	23.2–61.7	<.001	86.4±14.2	0–100	84 (91%)
	24 mo (n =73)	52.5±6.3	24.8–59.8	<.001	53.8±7.7	21.8–64.3	<.001	83.9±15.3	0–100	64 (88%)
	36 mo (n=61)	53.7±5.1	30.7–62.8	<.001	53.3±7.4	25.2–63.1	<.001	86.3±11.2	48–100	52 (85%)

Secondary Efficacy Endpoints

Fibroid and Uterine Volume

Uterine imaging by MRI or ultrasound for UFE patients did not extend past the 6-month follow-up. Uterine and fibroid volumes were calculated using the formula for the volume of a prolate ellipse (LxWxDx0.52). Significant decreases in both uterine volume (measured as including the cervix) and uterine fibroid volume were recorded for the UFE group by the 3-month evaluation, with further improvements seen at 6 months ($p<0.001$ at both time periods as compared to baseline). Table 5 summarizes the percent changes in uterine and fibroid volumes at 6 months following treatment. This table includes uterine volume data from 91 of the 108 UFE Phase II patients (84%) and fibroid volume data from 83 of these patients (77%) who had complete and evaluable imaging reports at baseline, and at 3 months and 6 months following UFE treatment. Increases in uterine volumes were reported for 11 patients (12%) and increases in fibroid volumes for 8 patients (8%) by the 6-month evaluation.

Table 5 – Percent Change in Uterine and Fibroid Volumes from Baseline

	% Decrease at 6 Months
Uterine Volume (cc)	
N	91
Mean	33.2% (30.5%)
Range	-93.6% to 82.0%
Fibroid Volume (cc)	
N	83
Mean	50.9% (41.7%)
Range	-173.4% to 99.7%

A positive percent change indicates a decrease in volume, while a negative percent change indicates an increase in volume.

Patient Satisfaction

Ninety-two of 100 UFE patients (92%) who completed the patient satisfaction questionnaire at 6 months were slightly, moderately or very satisfied with the outcome of their procedure, with the majority being very satisfied. Satisfaction remained relatively high three years after UFE treatment, with 52 out of 61 patients (85%) surveyed reported they were moderately or very satisfied.

ADVERSE EVENTS:

Adverse event data is reported for all 132 patients for up to 6 months after being treated by UFE (Table 6). There were no unanticipated adverse device effects or unanticipated adverse events reported in this study. Table 6 presents 51 adverse events judged to be probably or possibly associated with the procedure, which occurred in 37 of the 132 UFE patients (28%). Seven of the 51 events (14%) occurred during the UFE procedure, five (10%) between the procedure and hospital discharge, 17 (33%) from hospital discharge to 1 month post-procedure, 11 (22%) from 1 to 3 months post-procedure, 4 (8%) from 3 to 6 months post-procedure, and 7 (14%) greater than 6 months post-procedure. The most common adverse event was an allergic reaction or rash, which occurred in 8 of the 132 patients (6%), and which were generally judged by the treating physician to be related to the drugs or contrast agent used during the procedure. All reactions resolved spontaneously or with treatment. Four patients had hysterectomies following UFE, for an overall hysterectomy rate of 3%. One hysterectomy was performed at 2 months post-UFE due to sustained fever/possible infection. The other three were elective hysterectomies due to dissatisfaction with UFE outcome, which occurred at 2, 10, and 11 months post-UFE. One patient (<1%) had a repeat UFE after her uterine arteries were found to be patent.

Table 6 – Timing and Type of Probably or Possibly UFE-Related Adverse Events

Event Description	# of Patient Complaints	# of Events	Procedure	In Hospital	< 1 Month	1-3 Months	3-6 Months	> 6 Months
Hysterectomy following UFE	4	4				2		2
Allergic reaction/Rash	8	8	2	3	3			
Fibroid/Tissue passage or removal	5	6			2	3		1
Pain related adverse events	4	4			3	1		
Catheter/puncture site related injury	6	7	1	2	4			
Urinary Tract Infection/ Cystitis	3	4			1	1	1	1
Vaginal Infection/ Vaginatis	5	7			2	1	2	2
Vaginal Irritation/ Burning/Discharge	2	2			1	1		
Other	9	9	4		1	2	1	1
Total	**46**	**51**	**7**	**5**	**17**	**11**	**4**	**7**

*A total of 34 out of 132 patients (26%) experienced one or more adverse event in this study. The number of patients in this column reflects the fact that some patients experienced more than one adverse event.

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All indications

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Information on packaging:

Symbol	Designation
	Manufacturer: Name & Address
	Use by date: year-month-day
	Batch code
	Catalog number
	Do not resterilize
	Do not use if package is damaged
	Keep away from sunlight
	Keep dry
	Do not re-use
	Caution - Refer to Instructions For Use
	Non-pyrogenic
	Sterilized using steam
	Lower limit of temperature

All serious or life-threatening adverse events or deaths associated with use of Embosphere Microspheres should be reported to the U.S. Food and Drug Administration under the MedWatch program and to the device manufacturer. Information about the MedWatch program and forms for reporting adverse events can be obtained at www.fda.gov/safety/medwatch/howtoreport/ucm053074.htm or by calling toll free 888-463-6332. Reports to Merit Medical, Inc. can be made by calling toll free 800-394-0295.

Embosphere®

Microspheres

警示：联邦（美国）法律将此器械限制为由执业医生使用或订购。

适用范围：

栓塞微粒球在临床上用于栓塞血管，适用于动静脉畸形、血供丰富型肿瘤及症状性子宫肌瘤的栓塞治疗。

治疗子宫肌瘤的临床应用：

子宫肌瘤栓塞术 (UFE)是缓解女性因子宫肌瘤引起的大量月

经出血、盆腔疼痛或压迫和/或排尿功能障碍等症状治疗的

一种替代治疗方法。

产品描述：

Embosphere 微球是采用 Merit Medical 公司的专有微球技术开

发而成的栓塞材料系列产品之一。 本微球产品设计提供可控

的靶向栓塞治疗。

Embosphere 微球由丙烯酸聚合物浸渍于猪明胶制成， 具有生

物相容性、亲水性、不可再吸收性。

Embosphere 微球有多种不同标定尺寸可供选择。

装置包装：

- Embosphere 微球装于 20 毫升无菌预装注射器中， 包装于可撕小袋中。
- 每个注射器内为无菌、无热原生理盐水，含有约 1.0 毫升或 2.0 毫升含 Embosphere 微球。

以下禁忌症、警告、注意事项以及使用说明的内容首先均

为适用于所有适应症的信息（即血供丰富型肿瘤、动静脉畸

形、子宫肌瘤）， 其次再为特定适应症的信息（即 UFE 和

神经系统）。

禁忌症：

所有适应症

- 不能耐受栓塞手术的患者
- 由于血管解剖或血流原因无法置入导管或注入栓塞剂
- 存在或可能发生血管痉挛
- 存在或可能发生出血
- 存在严重的动脉粥样硬化疾病
- 供血动脉的直径的近端小于远端
- 存在侧支血管通路，栓塞时可能危及正常区域
- 病灶的供血动脉不够大，无法接受 Embosphere 微球
- 供血动脉的外周血管阻力较大， Embosphere 微球无法送入病灶
- 大口径的动静脉分流（即血液不通过动脉/毛细血管/静脉过渡，而是直接从动脉流入静脉）
- 肺部血管系统中

UFE 的特定禁忌症

- 孕妇
- 怀疑有盆腔炎或其他任何盆腔活动性感染者
- 骨盆区域有任何恶性肿瘤
- 子宫内膜瘤样病变或增生
- 有一个或多个粘膜下子宫肌瘤，其中50%以上已长入宫腔内
- 以带蒂浆膜肌瘤为主的子宫肌瘤
- 明显由侧枝血管而非子宫动脉供血的肌瘤

神经系统的特定禁忌症

- 存在通畅的颅外至颅内吻合或分流
- 存在直接汇入颅神经的终动脉
- Embosphere 微球可能直接进入颈内动脉、椎动脉、颅内血管或以上所列血管的任何脉管系统

警告：

所有适应症

- Embosphere微球含有猪明胶，因此，对胶原蛋白或 明胶敏感的患者可能出现免疫反应。 对于怀疑对含 有明胶稳定剂的注射液过敏的患者，使用本产品前应慎重考虑。
- 研究表明 Embosphere 微球不形成聚集体，因此与 同样大小的 PVA 颗粒相比，微球能够渗透到血管更深处。 为动静脉畸形、存在较大分流的患者进行栓塞时，必须谨慎选择较大尺寸的 Embosphere 微球，避免微球进入肺循环或冠脉循环。
- 部分Embosphere微球可能略超出治疗范围之外，因此医生一定要根据位于血管系统中所要栓塞层次 的靶血管大小，结合动静脉血管造影的结果慎重 选择 Embosphere 微球的大小。 必须选择合适的 Embosphere 微球大小，避免微球从动脉通入静脉。
- 由于误栓塞的并发症较严重，因此对环绕头部和颈部 的颅外循环的任何手术均应格外小心，并且医生应对 栓塞治疗的潜在益处与风险和潜在并发症进行仔细权衡。 其并发症包括失明、听力丧失、嗅觉丧失、瘫痪和死亡。
- 患者长时间、大范围暴露在透视下、以倾斜角度照射 X 光，并多次拍摄记录 X 光片，都可能因放射而引起 严 重的皮肤损伤。 请查阅您所在机构的临床方案，确保所进行的每一类具体操作均应用了适当的辐射剂 量。 医师应对可能存在风险的患者进行监测。
- 放射引起的损伤可能为迟发。应告知患者有关放射 的潜在副作用，并告知患者在出现症状时应与何人 联系。
- 应格外留意靶点外误栓塞的征象。注射过程中仔细监 测患者的生命体征，包括 SAO2（如缺氧、中枢神经 系统的变化）。 如果出现靶点外误栓塞的任何征象或患者发生症状，应考虑终止手术，检查可能存在的 分流或增加微球大小。
- 如果血管造影证实在微球注射过程中不能迅速出现明显栓塞， 则考虑加大微球尺寸。

UFE 的特定警告

与 UFE 和妊娠有关的警告

- 目前，UFE对女性的怀孕和怀胎至足月的能力以及胎 儿发育的影响还不明确。 因此，该手术只能为不打算再次怀孕的妇女实施。
- 在 UFE 之后怀孕的女性发生产后出血、早产、剖腹 产和先露异常 的风险可能增加。
- 理论上，UFE 阻断子宫肌层血流可能导致 UFE 术后 怀孕的女性 发生子宫破裂的风险增高。

其他 UFE 警告

- 使用 Embosphere 微球进行子宫肌瘤栓塞术时，不要 使用小于 500 微米的微球。
- 要接受子宫肌瘤栓塞术的患者都应接受适当的妇科检 查（如妇科病史、子宫肌瘤成像、月经异常出血患者 子宫内膜活检排除癌症）。
- 采取非手术方法（如 UFE）治疗子宫肌瘤可能会延误 子宫肉瘤 的诊断。 在推荐此类患者接受 UFE 之前，必须密切留意肉瘤的警告征兆（例如肿瘤生长迅速、
- 绝经后又出现子宫增大、MRI 表现），并进行更深 入细致的检查。 UFE 之后肿瘤复发或继续增长应视 为肉瘤的潜在征兆， 此时应考虑手术治疗。

使用小微球的警告

- 考虑使用直径小于您的成像设备分辨率的栓塞剂时，应格外谨慎。 动静脉吻合的存在、靶区域存在分支 血管或栓塞前显影不明显的血管可能导致靶点外误栓塞和严重并发症。
- 小于 100 微米的微球一般会迁移到血管吻合口远端，因此更有可能终止远端组织的血液供应。 使用较小 的微球可能有更大机会造成缺血损伤，因此栓塞前必须考虑到这种损伤的后果。 可能产生的后果包括 肿胀、坏死、瘫痪、脓肿和/或更严重的栓塞后综合征。
- 栓塞后肿胀可能会导致靶区域周围组织缺血。 必须注 意避开不能耐受缺血的非靶组织，如神经组织。

注意事项：

所有适应症

- 已知对造影剂过敏的患者在进行栓塞前可能需要接受糖皮质激素。
- 对于以下疾病的患者，围手术期护理管理中可能需要采取额外评估或预防措施：
  - 出血体质或高凝状态
  - 免疫功能低下
- 若注射器、柱塞密封或托盘包装出现破损，请勿使用。
- 仅供一名患者使用 - 内容物无菌 - 如注射器已打开，不得对内容物重复使用、再加工或再次灭菌。 重复使用、再加工或再次灭菌处理可能会损害装置的结构完 整性和/或使装置失效，从而可能导致患者受伤、生病或死亡。 重复使用、再加工或再次灭菌处理还可能带来污染风险并/或造成患者感染或交叉感染，包括（但不限于）将传染性疾病从一位患者传给其他患者。 装置污染可能会造成患者受伤、生病或死亡。所有操作均必须采用公认的无菌技术进行。
- 不要将装有 Embosphere 微球的 20 毫升注射器直接连接到微导管上进行输送，这样可能使导管阻塞。
- 本注射器仅供栓塞使用。 不要用于其他任何用途。
- 根据所要治疗的疾病选择适当的 Embosphere 微球大小和数量。
- 只有接受过所要治疗部位的介入栓塞培训的医生方可使用 Embosphere 微球实施栓塞治疗。

特定于 UFE 的注意事项

- 随着子宫动脉血流减少， Embosphere 微球逆向移动至非预期血管的几率会增高。 当子宫动脉血运完全停滞前，肌瘤周围的血管系统已不再可见时，应停止栓塞。
- 只能由接受过子宫肌瘤治疗的适当培训的介入放射科医师实施 UFE。

潜在并发症：

所有适应症

血管栓塞是一种风险高的手术。在手术期间或之后可能发生

并发症，并且可能包括但不限于以下：

- 靶点外部位栓塞导致麻痹，或因相邻组织水肿导致缺血性损伤。
- Embosphere微球有害回流或进入靶点病灶相邻的正常动脉，或通过病灶进入其他动脉或动脉床，如颈内动脉、肺动脉或冠状动脉循环等
- 由于动脉静脉分流而导致肺栓塞
- 非预期位置发生缺血，包括缺血性中风、缺血性梗阻（包括心肌梗阻），以及组织坏死
- 毛细血管床阻塞和组织损伤
- 血管或病灶破裂出血
- 血管痉挛
- 再通
- 需要医疗干预的异物反应
- 需要医疗干预的感染
- 插管相关并发症（如插管部位血肿、导管尖形成血凝块并随后脱落、神经和/或循环系统损伤等，均可能 导致腿部损伤）
- 对药物有过敏反应（如止痛药）
- 对造影剂或栓塞剂发生过敏反应
- 栓塞后可能出现疼痛和/或皮疹，症状发生时间可能滞后
- 死亡
- 失明、听力丧失、嗅觉丧失，和/或瘫痪
- 警告部分可看到更多信息

特定于 UFE 的潜在并发症

- 术后最常见的并发症是腹痛、不适、发烧和/或恶心，统称为 “栓塞后综合征。 部分患者也可能发生便秘。 该症状一般可采用处方药或非处方药治 疗。
- 卵巢早衰（即绝经）
- 闭经
- 骨盆区域感染
- 子宫/卵巢坏死
- 静脉炎
- 深静脉血栓形成，伴或不伴肺栓塞
- 阴道分泌物
- UFE 后组织排出、肌瘤脱落或肌瘤排出
- UFE 后介入以清除坏死的肌瘤组织
- 迷走神经反应
- 瞬态高血压发作
- 子宫切除术
- 截至 2002 年 11 月，全世界共有约 25,000 至30,000 名女性接受 UFE 治疗，其中已知有 4 例死亡，死亡率为 0.01% 至 0.02%。

神经系统的特定潜在并发症

- 缺血性卒中或缺血性梗死
- 神经功能障碍，包括颅神经麻痹

储存和无菌：

- Embosphere 微球必须装在原有的注射器和包装中，存放于阴凉、 干燥的避光处。
- 在注射器标签上标注的日期前使用。
- 请勿冷冻。
- 请勿再次灭菌。

使用说明：

使用前检查包装，确保其密封完整，产品保持无菌状态。

- 栓塞手术前采用高分辨率成像仔细评估病灶血管网。
- Embosphere 微球有多种尺寸可供选择。
- 由于误栓塞的可能性和微球大小固有的多样性，医生应确保根据血管网上所要的堵塞水平上靶血管大小慎重选择 Embosphere 微球大小。
- 栓塞动静脉畸形 (AVM) 时，应选择适当大小的 Embosphere 微球，使其既能阻塞病灶，又不会从动静脉畸形处通过。
- 进行子宫肌瘤栓塞术时，应选择 500 微米或更大的 Embosphere 微球。
- 根据靶血管和所用微球大小，选择合适的输送导管。Embosphere 微球可耐受高达 33% 的临时压缩，以便通过导管输送。
- 按照标准操作将输送导管送入靶血管。将导管尖放置在尽可能靠近治疗部位的位置，以避免意外阻塞正常血管。
- Embosphere 微球不透 X 光。 建议在生理盐水悬浮液中加入适量的造影剂，采用透视对栓塞过程进行可视化监测。

通过以下步骤输送 Embosphere 微球：

- 采用与注射器中总体积相同的未稀释造影剂，配制出50%微球/生理盐水和 50% 造影剂的溶液。 除净注射器中的所有空气。 将 20 毫升注射器轻轻颠倒几次，使Embosphere微球造影剂溶液悬浮均匀。 将 20 毫升注射器连接到鲁尔接头三通活塞的一端。在活塞另一端连接一个 1 毫升或 3 毫升注射器。如果需要的话，剩下的端口上还可连接输送导管。 等待几分钟，让Embosphere 微球在溶液中充分悬浮。 将 Embosphere微球/造影剂溶液缓慢、轻轻地抽取到注射器中，尽量避免向系统中带入空气。 注射前，清除系统中的所有空气。 在透视下采用缓慢搏动性注射将注射器中的Embosphere 微球/造影剂溶液注入，同时观察造影剂的流速。 如果流速没有变化，则再次注射 Embosphere微球/造影剂溶液重复输送操作。 如果首次注射后造影剂流速无变化，可考虑换用更大尺寸的 Embosphere 微球。 需要让 Embosphere 微球/造影剂溶液再悬浮时，将 20 毫升注射器轻轻颠倒几次。 在确定栓塞终点时应采取保守判断。
- 股骨穿刺可导致动脉痉挛。这容易导致股动脉血栓形成（例如腿部损伤）。最终拔除导管前，应重新评估股动脉通畅情况。
- 治疗完成后，在拔除导管的同时保持轻微的抽吸， 以免仍留在导管腔内的 Embosphere 微球脱落。
- 穿刺部位加压，直到止血为止。
- 丢弃任何打开但未使用的 Embosphere 微球

UFE 的其他特定说明：

- 医生可酌情决定为目前服用激素治疗、子宫体积>1000 毫升以及超重的患者使用充气加压装置，以降低深静脉血栓形成的风险。
- 肌瘤周围的血管系统已不再可见，但在子宫动脉血运完全停滞前，，应停止栓塞。 随着子宫动脉血流减少， Embosphere 微球逆向移动至非预期血管的几率 会增高。

UFE 患者咨询信息：

- 仅患者在接受栓塞治疗前应对提供术后护理的人员以及栓塞后发生紧急情况时的联系人有明确的认识。Merit Medical, Inc. 公司提供并分发患者须知手册。
- UFE研究对象应知晓与UFE相关的潜在益处，风险及不良反应。尤为重要的是，患者应悉知UFE手术有可能无法缓解与肌瘤相关的各种症状。

UFE 临床研究摘要：

研究设计

为了研究使用 Embosphere 微球治疗症状性子宫肌瘤的 UFE，我们进行了前瞻性多中心试验。在该研究中，共有 132 名希 望保留子宫同时避免外科手术的女性接受了 UFE 治疗；其中 30 名参与了初步可行性研究，102 名参与了关键研究。对关键 研究中包括的这些患者进行了为期 3 年的随访，分别对在治疗 后 3 个月、6 个月、12 个月、24 个月和 36 个月获得的结果进 行了临床评估。 七个调查地点参与了该研究。 该研究设计用于确定使用 Embosphere 微球的 UFE 是否能够减 轻与症状性肌瘤相关的症状，如异常出血、 疼痛、不适和泌 尿问题。

主要研究终点包括：

- 使用图示出血评估表测量从基线到UFE后6个月的经血量减少
- 使用患者症状调查问卷评估肿块占位症状（盆腔疼痛、盆腔不适/下腹膨胀和泌尿功能障碍）的改善程度
- 使用SF-12健康状况调查问卷评估生活质量的改善程度

次要终点包括：

- 经血变化的其他指标
- 子宫和肌瘤体积减小
- 住院时间
- 恢复正常活动所需的时间
- 评估患者对手术的满意度

还评估了不良事件和并发症的类型、比率及严重程度。

入组标准包括：年龄 30 至 50 岁（含）、不育或没有计划怀孕、 存在一个或多个症状性子宫肌瘤、子宫体积 ⩾ 250 毫升或肌瘤体积 ⩾ 4 毫升和基线 PBLAC ⩾ 150。以下女性被排除在研究之外：怀孕女性、有盆腔炎病史、粘膜下子宫肌瘤宫腔内增长已超过 50%、以带蒂浆膜肌瘤为主的子宫肌瘤、明显由侧枝血管而非子宫动脉供血的肌瘤、子宫腺肌病为症状主因者、子宫内膜增生或癌前增生、骨盆区域有任何恶性肿瘤、骨盆区域有任何活动性感染、已知对静脉造影剂或明胶过敏、出血体质，免疫功能低下、绝经后或基线 FSH >40mIU/毫升，或之前3个月内曾接受 GnRH拮抗剂治疗的。

治疗前评估包括常规妇科检查和化验、标准实验室化验、 超声波或 MRI、经血记录（UFE 组），以及与总体健康状况 (SF-12)、经血和肌瘤症状相关的自我评估调查问卷。

研究结果

在报名参加关键研究的 102 名患者中，有 96 名患者拥有完整 的基准数据，有 69 名 (72%) 在 UFE 治疗 3 年后具有已知结果。 并非所有患者都在最终随访间隔中提供了所有结果测量值， 下面的各表中详细列出了参与各阶段随访的患者数量。

治疗过程、分泌物和恢复信息

技术上而言，所有可行性研究和关键性研究的UFE手术均成功完成，术中没有发生使手术无法完成的并发症。 大部分(77%)UFE手术采用5Fr导管进行，其余则采用4Fr(19%)或3Fr(3%)进行。72 名患者采用500-700微米的微球治疗，66名采用700-900微米的微球治疗，18名采用900-1200微米的微球治疗。 多数患者均采用多于一种尺寸的微球进行治疗。最常用的治疗方法是从尺寸较小的微球开始，如有必要再增加尺寸。治疗所需要的微球体积与所用的微球大小成反比，平均而言，500-700微米的微球需要使用7.2毫升，而700-900微米的微球需要6毫升，900-1200微米的微球需要4.1毫升。

大多数UFE患者的手术均在穿刺部位局麻下完成，术中患者保持清醒镇静。所有UFE手术均未在全身麻醉下进行。按开始动脉穿刺到最终拔除导管的时间计算，UFE手术的平均时间为58±28分钟（范围为 10到140分钟）。87%的UFE患者在栓塞后第二天出院，12%于手术当天出院。UFE患者平均恢复在10.7天后返回工作岗位，或者恢复正常日常活动。

主要疗效终点

经血

此项研究 UFE 患者的入组标准是必须有大量异常月经出血、基线 ⩾ 图示月经出血量评估表 (PBLAC)评分为 150（Janssen等人，1995）。治疗成功被定义为 ⩾ 治疗后 6 个月随访评估时PBLAC评分减少50%。研究还采用患者自我评估出血水平和月经过多问卷等其他指标来评估经期出血的变化。UFE后，月经出血情况通常迅速发生变化，92%的患者在3个月时症状即有改善。 通常会在 UFE 后迅速出现经血变化，其 中 92% 的患者到 3 个月时显示出症状改善。在参加关键研究 的 102 名患者中，只有 48 名患者在 36 个月时填写了经血过 多调查问卷，并且只有 41 名患者提供了配对数据。但结果表 明，得分出现了实质性且具有统计学意义的显著改善（分数 越低越好），并且在该研究随访过程中，平均得分持续改善 （表 1）。这些结果与患者经血自我评估（表 2）完全一致。 在基线上，54% 的患者将其出血水平评为“极多”，42% 的 患者将其出血水平评为“中等”。在为期 36 个月的随访过程 中，只有 3% 或以下的患者将其出血水平评为“极多”，不超 过 28% 的患者将其出血水平评为“中等”。在治疗后 36 个月 时，22% 的患者指出其没有月经期。

表 1 – 经血过多调查问卷的结果

		所有数据		配对数据 (n=41)*	
		平均分标准差	范围	平均分标准差	范围
治疗前 (n=96)		47.9±13.1	14.29-83.33	45.2±13.5	14.3-83.3
治疗后	3 个月 (n=83)	24.5±13.1	7.1-64.3	22.9±10.7	7.1-54.8
	6 个月 (n=83)	21.03±11.9	7.1-64.3	18±8.6	7.1-52.4
	12 个月 (n=78)	17.1±10.1	2.4-61.9	18.6±11.7	2.4-61.9
	24 个月 (n=67)	19.7±11.8	0-54.8	17.8±9.4	0-54.8
	36 个月 (n=48)	19.2±11	0-57.1	20.1±10.7	0-57.1

注—每段时间间隔的得分与基准线上的得分之间的差异在统计学上非常显著 (P <.001)。P 值是通过检验、配对检验和符号检验计算得出的。 * 配对数据来自在每次随访间隔时都提供了数据的患者(n=41)。

表 2 – 患者经血评估。

		出血描述				
		极多	中等	正常	较少	没有月经期
治疗前 (n=95)		54 (57)	40 (42)	1 (1)	0 (0)	0 (0)
治疗后	3 个月 (n=87)	3 (3)	38 (44)	27 (31)	13 (15)	6 (7)
	6 个月 (n=88)	3 (3)	25 (28)	37 (42)	18 (20)	5 (6)
	12 个月 (n=83)	1 (1)	17 (20)	38 (46)	21 (25)	6 (7)
	24 个月 (n=71)	2 (3)	17 (24)	33 (46)	15 (21)	4 (6)
	36 个月 (n=59)	1 (2)	14 (24)	27 (37)	9 (15)	13 (22)

注— 数据以患者人数的方式提供。括号中的数字为百分比。

与占位相关症状

大部分患者的疼痛、不适和泌尿问题等与占位相关症状 （表 3）都得到了显著改善，不过每个数据间隔时泌尿症状显 著改善的患者人数较少。

表 3 – 与占位 相关症状的状态：进行栓塞治疗后出现中等到显 著改善的患者所占比例

	症状		
	盆腔疼痛	盆腔不适	泌尿问题
3 个月 (n=86)	63 (73)	61 (71)	46 (53)
6 个月 (n=87)	68 (78)	71 (82)	58 (66)
12 个月 (n=81)	77 (83)	67 (81)	56 (69)
24 个月 (n=73)	60 (83)	61 (83)	44 (62)
36 个月 (n=59)	49 (83)	49 (83)	42 (69)

注— 数据以患者人数的方式提供。括号中的数字为百分比。

生活质量

我们使用 SF-12 健康状态调查问卷，对治疗后的一般生理和 心理健康状态的变化进行了评估。此终点的目标是证明总体 生活质量中出现至少一

项中等改善。SF-12 健康状态调查问卷 的结果显示在表 4 中。此调查问卷包含 12 个问题，计分并针 对美国总体人口规范化至平均分为 50 分，标准差为 10。对于 进行栓塞治疗前的患者，平均生理和心理总结得分为 45 分。 生理总结得分在 3 个月时提高到 51.8 分，在 36 个月时提高到 53.7 分；而平均心理得分在 3 个月时为 52.1 分，在 36 个月时 为 53.3 分。患者的健康状态认知也相应提高了，在 36 个月 时，从平均 69.5 分提高到 86.3 分。在该研究结束时，84% 的 患者对该治疗过程的症状控制感到非常满意或比较满意。

表 4 – 与总体健康状态和结果满意度相关的 SF-12 调查问卷结果

		评估的参数								
		生理状态			心理状态			总体健康状态		比较满意或非常满意的患者人数
		平均分标准差	范围	*P* 值	平均分标准差	范围	*P* 值	平均分标准差	范围	
治疗前	(n=96)	45±8.3	26-61.6		45±11.5	22.3-63.4		69.5±19.1	0-100	
治疗后	3 个月 (n=88)	51.8±6.7	22.3-58.5	<.001	52.1±7.7	23.8-61.6	<.001	82.6±14.2	28.7-100	78 (89%)
	6 个月 (n=88)	52.4±6.2	23.3-62.6	<.001	52.9±7.9	20.5-60.8	<.001	85.1±11.3	43.8-100	78 (89%)
	12 个月 (n=82)	53.6±5.9	23.1-64.1	<.001	52.6±7.8	23.2-61.7	<.001	86.4±14.2	0-100	84 (91%)
	24 个月 (n=73)	52.5±6.3	24.8-59.8	<.001	53.8±7.7	21.8-64.3	<.001	83.9±15.3	0-100	64 (88%)
	36 个月 (n=61)	53.7±5.1	30.7-62.8	<.001	53.3±7.4	25.2-63.1	<.001	86.3±11.2	48-100	52 (85%)

次要疗效终点

肌瘤体积和子宫体积

在为期 6 个月的随访后，UFE 患者的 MRI 或超声波子宫影像并 未增大。使用扁长椭圆体积公式 (LxWxDx0.52) 计算子宫体积和 肌瘤体积。记录表明，对于 UFE 组，在 3 个月评估时无论是 子宫体积（测量时包括子宫颈）还是子宫肌瘤体积都显著减 小；在 6 个月时发现进一步改善（与基准相比，在两个时间 段的 p 值均小于 0.001）。表 5 概述了子宫体积和肌瘤体积在 治疗后 6 个月时的变化百分比。此表包括了来自 108 名 UFE 二期患者中的 91 名患者 (84%) 的子宫体积数据，以及这些患 者中拥有完整且可评估的基线及 UFE 治疗后 3 个月和 6 个月时 的影像报告的 83 名患者 (77%) 的肌瘤体积数据。报告表明， 在 6 个月评估时，11 名患者 (12%) 的子宫体积增大，8 名患者 (8%) 的肌瘤体积增大。

表 5 – 子宫体积和肌瘤体积与基准相比的变化百分比

	在 6 个月时减小的百分比 (%)
子宫体积 (cc) N 平均值 范围	 91 33.2% (30.5%) -93.6% 至 82.0%
肌瘤体积 (cc) N 平均值 范围	 83 50.9% (41.7%) -173.4% 至 99.7%

变化百分比为正表明体积减小，而变化百分比为负则表明体积增大。

患者满意度

在填写 6 个月时患者满意度调查问卷的 100 名 UFE 患者中，有 92 名患者 (92%) 对其治疗过程的结果表示略微满意、比较满意 或非常满意，其中大部分为非常满意。在 UFE 治疗后 3 年时， 满意度仍保持相对较高的水平，在 61 名接受调查的患者中， 有 52 名患者 (85%) 报告他们比较满意或非常满意。

不良事件：

报告了全部 132 名患者的不良事件数据，最长时间为进行 UFE 治疗后 6 个月（表 6）。在此研究中，并未报告非预期的装置不良反应或非预期的不良事件。表 6 显示了 51 起不良事件，根据判 断，这些不良事件可能与该治疗过程相关，在 132 名 UFE 患 者中，有 37 名患者 (28%) 发生了这些不良事件。在这 51 起事 件中，7 起 (14%) 发生在 UFE 治疗过程中，5 起 (10%) 发生在该 治疗过程与出院之间，17 起 (33%) 发生在从出院到治疗过程后 1 个月期间，11 起 (22%) 发生在从治疗过程后 1 个月到 3 个月 之间，4 起 (8%) 发生在从治疗过程后 3 个月到 6 个月之间，还有 7 起 (14%) 发生在治疗过程后 6 个月之后。最常见的不良事 件为过敏反应或皮疹，在 132 名患者中，有 8 名患者发生了此 类不良事件 (6%)，治疗医生大体判断此类不良事件与该治疗 过程中使用的药物或造影剂相关。所有反应都已自发解决， 或者通过治疗得到了解决。4 名患者在 UFE 后进行了子宫切除 手术，总体子宫切除率为 3%。1 例子宫切除手术是在 UFE 后 2 个月时由于持续发热/可能感染而执行的。另外 3 例属于选择 性子宫切除手术，原因在于对 UFE 结果不满意，分别是在 UFE 后 2 个月、10 个月和 11 个月时执行的。1 名患者 (<1%) 在发现 其子宫动脉再通后，重复进行了一次 UFE。

表 6 – 可能与 UFE 相关的不良事件的发生时间和类型

事件描述	患者投诉数量	事件数量	治疗过程	住院期间	1 个月以内	1-3 个月	3-6 个月	6 个月以上
UFE 后的子宫切除手术	4	4				2		2
过敏反应/皮疹	8	8	2	3	3			
肌瘤/组织流出或移除	5	6			2	3		1
与疼痛相关的不良事件	4	4			3	1		
与导管/穿刺部位相关的损伤	6	7	1	2	4			
尿路感染/膀胱炎	3	4			1	1	1	1
阴道感染/阴道炎	5	7			2	1	2	2
阴道刺激/烧灼感/分泌物	2	2			1	1		
其他	9	9	4		1	2	1	1
合计	**46**	**51**	**7**	**5**	**17**	**11**	**4**	**7**

*在此研究的 132 名患者中，共有 34 名患者 (26%) 经历了一起或多起不良事件。 此列中的患者人数反映了有些患者经历了一起以上的 不良事件的事实。

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