

## **Advances in Vascular Interventions: Uterine Fibroid Embolization**

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### Clinical background

Uterine leiomyomata, commonly known as fibroids, are an extremely common benign lesion; they are present in 30-50% of all women, with a slightly higher incidence in women of African descent. Symptoms (menometrorrhagia, pain, compression of adjacent structures) occur in roughly 50% of women with fibroids (25% of all women). While medical management can reduce these symptoms, definitive treatment has historically required surgical intervention: in the United States alone, fibroids are responsible for up to 200,000 hysterectomies annually. The physical bulk of fibroids frequently mandates an open abdominal approach, with significant morbidity. Other surgical options exist, including myomectomy and electrocautery coagulation (myolysis), but each has its limitations. The rate of fibroid recurrence after myomectomy is as high as 10% per year over the first five post-operative years and 25% of women treated with myomectomy eventually require additional treatment. Myolysis, though less invasive than myomectomy, is nonetheless a surgical procedure requiring general anesthesia, and might be expected to have recurrence rates similar to those of myomectomy (confirmatory data are not yet published).

### Premise of UAE as a definitive treatment

- Uterine fibroids are benign hypervascular tumors that occasionally undergo spontaneous infarction
- After spontaneous infarction, fibroids are often seen to undergo involution and volume reduction.
- Iatrogenic infarction (by percutaneous catheter embolization) duplicates this naturally occurring process with similar results.

### Historical perspectives

Embolization of the uterine artery in treatment of gynecologic malignancy or trauma is a well-established procedure dating back to the 1970's. As with other embolization procedures, the first agent used was autologous clot. Coils, glues, and particulate emboli have all been used since. The concept of elective preoperative UAE, using polyvinyl alcohol, was introduced Ravina et al (France) in a 1994 letter to Presse medicale. The same group went on to describe the successful use of UAE as a definitive treatment for fibroids in 1995. Other reports, duplicating Ravina's results, were published in 1997. Since then, interest in the procedure has increased geometrically, with extensive coverage in both peer-reviewed and lay press and on the Internet. Worldwide experience to date is roughly 15,000 cases, with the largest individual series being just over 1,000 cases by Rob Worthington-Kirsch (Philadelphia).

### Published and reported outcomes

Reported technical success (bilateral uterine arterial occlusion) is over 95%. Reported clinical success (symptom relief) ranges from 80% to greater than 90%, with fibroid and uterine volumes reduced by 40-80% (median roughly 50%) over a period of 6 months and patient satisfaction ranging from 75-100%. Perioperative morbidity is extremely low, especially when compared to hysterectomy or abdominal myomectomy; while most UAE procedures are followed by overnight admission, several operators have reported success with same-day (outpatient) management. Complication rates are also extremely low, though complications have been reported (discussed below). Significantly, there have to date been no reported cases of late symptom recurrence or fibroid growth after clinically successful UAE.

### Reported complications

Moderate to severe pain is present in nearly 100% of cases, but is variable in degree and relatively short-lived (discussed further below). Post-embolization syndrome (fever, leukocytosis, malaise) develops in roughly 30% of cases, generally beginning 3-5 days after treatment and lasting 1-5 days. Transient or permanent amenorrhea has been reported in up to 15% of all women and up to 43% of women over the age of 45. While no definitive etiology for this finding has been determined, the most likely factor appears to be ovarian and/or endometrial ischemia rather than radiation injury. Sloughing and transvaginal expulsion of submucosal fibroids have been reported, and may occur in roughly 5% of cases. Other complications, including uterine infection/infarction, pulmonary embolism, and symptomatic "non-target" embolization have been reported, but are distinctly uncommon.

### Patient selection

- Pre-procedure requirements
  - thorough, current gynecologic evaluation to verify the etiology of symptoms and exclude other diagnoses (malignancy)  
***this procedure must not be performed without such an evaluation.***
  - current ultrasound or MRI documenting fibroid size
  - exclusion of pregnancy, occult infection
- Ideal Patient Profile
  - is pre-menopausal no longer desiring fertility, or post-menopausal with failure to regress spontaneously
  - has failed medical management
  - has an absolute or relative contraindication to surgery (including patient preferences)
  - has a fibroid of moderate size (3-7 cm)
- Poor Candidate Profile
  - has minimal symptoms, or symptoms easily controlled by medical management
  - desires fertility, and is amenable to myomectomy
  - has primary complaint of spontaneous abortion
  - has an isolated pedunculated submucous fibroid
  - requires other pelvic surgery

### Contraindications

- absolute:
  - pregnancy
  - known or suspected pelvic infection or bacteremia
- relative:
  - coagulopathy, renal failure, or contrast allergy
  - peripheral vascular occlusive disease
  - current therapy with Lupron or similar agents

### General UAE Technique

- Foley catheter
- Conscious sedation (some use epidural analgesia, but there is no role for general anesthesia)
- Unilateral or bilateral groin access with 4 or 5 F catheter
- Selective catheterization of each uterine artery, sometimes requiring a coaxial microcatheter
- Embolization with particulate materials (200-700  $\mu\text{m}$  size) sometimes followed by gelfoam
  - The ideal endpoint has not been established and likely varies by embolic agent
- Post-procedure pain management with PCA pump or epidural (most admit overnight, many do not)
- Follow-up visit with primary provider within one month
- Follow-up imaging at three, six, and 12 months; additional imaging as clinically indicated

### Anatomic and physiologic considerations

In most cases, the paired uterine arteries are the dominant source of blood flow to uterine fibroids. The uterine artery arises from the anterior division of the internal iliac artery. In a woman without fibroids, the artery is generally not seen during non-selective pelvic arteriography. When fibroids are present, however, the uterine artery dilates and takes on a readily identifiable configuration. There is often a great deal of tortuosity at the origin, and catheter-induced spasm is commonly seen. In many cases, selective uterine arteriography will demonstrate a prominent branch to the cervix; most agree that this vessel should be spared if it can be identified. Variant anatomy has been described, including multiple duplication and congenital absence or hypoplasia. In the latter condition, replacement to the ipsilateral ovarian artery may be present. Even with large, patent uterine arteries, collateral supply from the ovarian arteries is not uncommon. Collaterals may also be present through adhesions. Failure to treat all significant sources of blood flow will reduce the likelihood of success. At a minimum, both uterine arteries should be treated.

The pattern of blood flow changes during embolization. Thus, if one of the arteries is initially difficult to catheterize, it may be useful to treat the other first: once the dominant supply is occluded, the secondary vessel may dilate and be more easily catheterized. Similarly, while collateral communications may not initially be evident, these channels can be at risk for reflux and non-target embolization once antegrade flow into the fibroid slows.

### Predictors of failure

- uterine artery anomalies
  - previous surgical ligation
  - variant anatomy
  - collaterals (previous pelvic surgery?)
- comorbid factors as the true etiology of symptoms
  - endometriosis
  - adenomyosis
  - pelvic venous congestion

### What happens to the fibroid?

- Immediate ischemia and subsequent infarction
- Hyaline sclerosis (coagulative necrosis), rather than liquifactive necrosis
- Moderate inflammation (this is the putative etiology for post-embolization syndrome)
- Progressive dehydration with retraction and volume reduction
- Occasional sloughing (especially common in the pedunculated submucosal type of fibroid)

### What happens to the uterus?

- Minimal embolization of myometrium and basal endometrium
  - preferential flow to hypervascular fibroids
  - myometrial perforating vessels smaller than the main trunk
- Minimal effect when embolization occurs
  - recruitment of flow from other pelvic vasculature?
  - recanalization of the uterine arteries?
- Infarction/infection rare, but reported
- No reports of uterine rupture

### What happens to the particles?

- PVA and acrylic microspheres are permanent embolic materials
  - no delayed reactions reported
  - no delayed migration
- Gelfoam is temporary (days to weeks)
  - localized vasculitis
  - ? advantageous in patients desiring fertility
- Glues and other agents under investigation; unknown future role

### Do fibroid size, location, or number predict outcome?

- Because the median volume reduction is roughly 50%, a larger initial size means larger final size. There is anecdotal evidence that fibroids greater than 8 cm may not reduce in size enough to relieve symptoms. This does not mean that larger fibroids cannot be treated successfully, but one should consider the following:
  - did the patient have symptoms when the fibroid was much smaller than at the time of assessment for UAE? If so, this might predict failure.
  - would moderate volume reduction facilitate less invasive surgery? If so, an attempt at UAE may be warranted because even if symptoms persist, the patient would have gotten some benefit.
  - avenue for investigation: does symptomatic response to lupron predict UAE outcome?
- Again anecdotally, there is some evidence that pedunculated lesions and subserosal lesions reduce less than do interstitial and submucosal lesion.
- The number of fibroids does not have any clear relationship to outcome

### Is it painful?

- Pain is extremely variable and difficult to predict, but can be significant.
- Onset is delayed, with pain beginning at the end of, or after, embolization
- Duration varies (3-10 days), but usually begins to diminish after reaching a peak 12-24 hours post-embolization
- Does not appear to vary with fibroid size, number of emboli, or particle size
- May be decreased when the embolization is performed with calibrated microspheres
- Does not appear to predict clinical outcome

### Pain management

- Because pain does not develop until the procedure is over, general anesthesia not indicated (epidural?)
- Versed, Fentanyl, and Toradol routinely during UAE procedure; morphine as needed
- PCA pump is very useful afterward embolization (morphine or demerol), with rates dependent upon pain level
- We usually discharge with Vicodin, Toradol, a laxative, and an antiemetic

### Is (safe) fertility maintained? (observations in favor)

- Historical evidence clearly shows that interruption of the uterine artery does not reduce fertility
- Several dozen post-UAE pregnancies have been anecdotally reported, and 12 recently published
  - No IUGR
  - No uterine ruptures, even among women having vaginal delivery
  - No fibroid recurrence during or after

### Is (safe) fertility maintained? (observations against)

- 5-43% Risk of permanent amenorrhea after UAE (increasing risk with age)
- In the published series, 5 of 12 pregnancies ended in early miscarriage (though median maternal age was 40)
- Unavoidable (though small) radiation dose to oocytes
- Many unknown variables
  - Unknown denominator (how many women are actually trying to become pregnant?)
  - Unknown risk of uterine rupture (too few currently reported cases)
  - Unknown effectiveness versus myomectomy in patients with spontaneous abortion

### Is it experimental?

- Embolization, as a technique, is not experimental. It is a well established approach to the control of bleeding in trauma and malignancy and in the palliative management of malignancy.
- Embolization of the uterine artery is also well established for these indications.
- Nonetheless, many questions exist regarding *elective* UAE for benign disease, and these are under investigation:
  - what is the best agent?
  - what is the best particle size?
  - what is the appropriate endpoint?
  - what is the long-term recurrence rate?
  - what is the role of UAE in patients desiring fertility?
  - who are the most appropriate patients?

### How much time/radiation are involved?

Dosimetry has been evaluated by several authors. All agree that the dose is low, but highly susceptible to anatomic, technical, and procedural variables.

- Patient-dependent factors
  - body habitus (dose is higher to heavier patients)
  - fibroid size (larger fibroids increase dose both by increasing radiographic density and by increasing the time required to achieve stasis).
  - arterial anatomy (increased screening time with difficult or multiple catheterizations)
- Operator-dependent factors
  - experience
  - technique

### Techniques to reduce dose

- Minimize image acquisition
- Raise the table to the highest comfortable working level
- Limit magnification
- Use pulsed or low-dose fluoroscopy
- Verify the effects of roadmapping

### Conclusions

- UAE is a safe procedure
- Clinical and imaging follow-up shows excellent results in appropriately selected patients
- Long-term outcomes await study, but the rate of symptom recurrence appears to be less than of myomectomy
- Fertility probably preserved in younger patients (<45 years), but may not be improved

More information

- Internet sites (general information)
  - [www.SCVIR.org](http://www.SCVIR.org)
  - [www.OHSU.edu/dotter-fibroid](http://www.OHSU.edu/dotter-fibroid)  
(AKA [www.fibroidembo.com](http://www.fibroidembo.com))
- Internet sites (chat/support)
  - [www.egroups.com/embo](http://www.egroups.com/embo)
  - [www.egroups.com/uterinefibroids](http://www.egroups.com/uterinefibroids)
- Patient pamphlets
  - available through SCVIR

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