Uterine Fibroid Embolization
History

- First UFE in 1995 in Ravina, France
  - 16 patients (34 - 48 yrs)
  - 100% technical success
  - 20 month follow-up
    - 11 complete response
    - 3 partial improvement
    - 2 failures
    - 14 experienced pelvic pain


- First UFE in the U.S. – 1997 at UCLA with Scott Goodwin, MD, and Bruce McLucas, MD


Types of Uterine Fibroids

- Intramural fibroid
- Subserosal fibroid
- Submucosal fibroid
- Pedunculated submucosal fibroid
- Pedunculated subserosal fibroid
Vascular Network

Arterial network measured in microns

<500µm

500-1000µm

1000-1500µm

Uterine artery
Accessing the Uterine Artery
November 2002 - First FDA Cleared Embolic Indicated for Uterine Fibroids
Angiographic X-ray of Pelvis
Angiographic Images of Fibroids

Pelvic Angio

Fibroid Blood Supply

Uterus

Fibroid
Targeted UFE

- Injection of Embosphere® Microspheres continues until you see no hypervascular tumor, pruned appearance in the feeder network, and slow flow in the uterine artery
- Stasis will be seen in the feeders
- Post image will show enhanced fibroids and normal myometrial perfusion
Targeted UFE – Pre UFE

Fibroid blood supply - uterine artery

Fibroid blood supply - uterine artery
The Process

Targeted Uterine Fibroid Embolization

1. Start embolization

2. Mid-point embolization

3. Mid-Upsize embolization

4. End embolization
   patent ovarian artery
Angiogram of fibroids before UFE (steps 1-3) and after UFE (steps 4-5)
Pre- & Post-Embolization with Embosphere® Microspheres

Images courtesy of James B. Spies, M.D., Georgetown University Medical Center
Pre- and Post-embolization with Embosphere® Microspheres

Growing Fibroids

Before UFE

Shrinking Fibroids

3 months Post UFE

Images courtesy of James B. Spies, M.D., Georgetown University Medical Center
Alternatives to Hysterectomy in Management of Leiomyomomas

“Based on long and short-term outcomes, uterine artery embolization is a safe and effective option for appropriately selected women who would like to retain their uteri.”

Level A evidence: good and consistent scientific evidence

ACOG 2008 Guideline

REST Trial

- Randomized multi-center study in the UK
- 2:1 ratio of UFE to surgery patients
  - UFE - 106 patients
  - Surgery - 51 patients
    - Hysterectomy – 43 patients
    - Myomectomy – 8 patients
- Primary outcome measured scores on SF-36 at 1 year

REST Trial - continued

• Short-term Results
  – UFE less painful 24 hours (VAS of 3.0 vs 4.6, P < .001)
  – UFE shorter stay (1 vs. 5 days, P<.001)
  – Return to work (20 vs 62 days, P<.001)
  – No difference in adverse events:
    • Major events (15% UFE vs 20% surgery, P=.22)
    • Minor events (34% UFE vs 20% surgery, P=0.47)
REST Trial

• Mid-term Results (median follow-up 32 months)
  – No difference in SF-36 QOL domain scores @12 months
  – No difference in EuroQol scores @12 months
  – Better improvement scores for surgery @12 months
    • Range: -5 markedly worse to +5 markedly improved
    • 4.3 for surgery vs 3.6 for UFE, P=.03
  – Both groups equally satisfied
    • Would recommend to friend: 88% for UFE vs 93% surgery, P=.32
  – UFE more likely to need re-intervention (21 for UFE vs 1 for surgery, P<.001)
    • 10 in first year, 11 in subsequent follow-up

Emmy Trial

- Randomized trial of hysterectomy vs UAE completed in Netherlands
  - 8 published papers since November 2005 on short-, mid- and long-term outcomes
    - Non-inferiority Trial
  - 177 patients (88 UAE, 89 hysterectomy) recruited in 34 centers
  - Participant recruited from among patients who had agreed to hysterectomy

Emmy Trial – continued

- Key findings: Short-term
  - No difference in SIR major complications (4.9% vs 2.7%, p=0.68)
  - More frequent minor complications with UAE (58% vs 40%, p=.024)
  - Higher re-admission for UAE (11.1% vs 0%, p=.003)

Emmy Trial – continued

• Higher than previously reported failure rate for UAE
  – Technical failure rate 5.3%
  – Procedural failure 17.3%

• Two year follow-up findings:
  – Using a series of QOL measures, including the SF36 MCS and PCS summary scores:
    • Quality of life for both groups significantly improved and not different between the groups
    • Patient satisfaction with outcome greater with hysterectomy than uterine embolization

Emmy Trial

Emmy Trial - continued

• Primary outcome is non-inferiority of UFE at 2 years
  – Hysterectomy avoided in at least 75% of patients

• Of the total UFE patients, 24% went on to hysterectomy

• Conclusion: the outcome from uterine embolization is not inferior to hysterectomy

Mara Trial

- Sixty-three patients randomized
  - 30 UFE
  - 33 myomectomy (15 lap, 18 open)
  - Mean age 32 both groups

- Short term:
  - UFE shorter stay (3.7 days vs 5.3, p<0.001)
  - UFE shorter recovery (13.6 days vs 30, p<0.0001)
  - No difference in:
    - Major complications (UFE 10% vs myo 3%)
    - Basal FSH after treatment (UFE 7.9 IU vs myo 6.5 IU, NS)
    - Proportion with symptomatic relief (UFE 87.5 vs myo 93.3%)

Randomized Study – Prague Trial

**Prague Trial**

- **Mid-term results**
  - 121 patients randomized UFE vs Myomectomy
    - Myomectomies: 63
    - UFE: 58
  - Follow-up: 118 pts - Minimum 12 months, mean 24.9 months

- **Most clinical outcomes no difference**

- **UFE higher re-intervention**
  - 36% vs 6.1%, p=0.01
  - Re-intervention routine on UAE if persisting fibroid >5cm, or recurrent fibroid in UFE or myomectomy >5 cm

## Reproductive Outcomes

<table>
<thead>
<tr>
<th></th>
<th>UFE</th>
<th>Myomectomy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant/Tried to conceive (N)</td>
<td>13 / 26</td>
<td>31 / 40</td>
<td></td>
</tr>
<tr>
<td>Pregnancy Rate</td>
<td>50%</td>
<td>78%</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Delivery Rate</td>
<td>19%</td>
<td>48%</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>Abortion Rate</td>
<td>64%</td>
<td>78%</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td>RR not to get pregnant after UFE</td>
<td>2.22 (95% C.I. 1.11 &lt; RR &lt; 4.44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR not to deliver</td>
<td>1.54 (95% C.I. 1.08 &lt; RR &lt; 2.18)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR to abort</td>
<td>2.79 (95% C.I. 1.25 &lt; RR &lt; 6.22)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The FIBROID Registry - Enrollment

- Initially 3,319 patients treated at 72 enrolling sites
  - 3,166 (95.4%) consented to Registry
  - Complete variables in 3,005 (94.9%)

- 30-day follow-up complete in 2,729 (90%)
- 2,112 eligible for long-term follow-up
- Six-month follow-up completed in 1,797 (85.1%)
- 12-month follow-up completed in 1,701 (83%)
The FIBROID Registry - Symptom Scores

<table>
<thead>
<tr>
<th>Symptom Score Mean</th>
<th>Baseline N = 2666</th>
<th>6 months N = 1797</th>
<th>12 months N = 1701</th>
<th>Normal population score</th>
</tr>
</thead>
<tbody>
<tr>
<td>59.83 (20.8)</td>
<td>19.87 (18.6)</td>
<td>19.23 (17.9)</td>
<td>22.5 (21.1)</td>
<td></td>
</tr>
</tbody>
</table>

Used with permission by James B. Spies, MD, MPH, Georgetown University School of Medicine, Washington, DC
The FIBROID Registry – HRQOL Scores

<table>
<thead>
<tr>
<th></th>
<th>Baseline N = 2666</th>
<th>6 months N = 1797</th>
<th>12 months N = 1701</th>
<th>Normal population score</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRQOL Score Mean</td>
<td>47.32 (22.9)</td>
<td>85.0 (20.1)</td>
<td>86.7 (18.1)</td>
<td>86.4 (17.7)</td>
</tr>
</tbody>
</table>

Used with permission by James B. Spies, MD, MPH, Georgetown University School of Medicine, Washington, DC
• Definition for long-term used for review:
  – Mean (median) of 36 months or greater at follow-up

• Reviewed
  – Long-term symptom control
  – Patient satisfaction
  – Rates of Recurrence
    • Hysterectomy, other interventions
<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>Duration of Follow-up</th>
<th>% with Symptom Control</th>
<th>Hysterectomy Rate</th>
<th>Recurrence Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katsumori T, Kasahara T, Akazawa K. AJR 2006;186:848-854</td>
<td>96</td>
<td>37.4 months</td>
<td>89.5%</td>
<td>3%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Bucek RA, Puchner S, Lammer J. AJR 2006;186:877-882</td>
<td>62</td>
<td>36 months</td>
<td>60%-89.5%</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

*Defined as recurrence of symptoms leading to the need for hysterectomy, myomectomy or repeat UAE greater than 12 months after treatment.
## Long-Term Outcome

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>Duration of Follow-up</th>
<th>% with Symptom Control</th>
<th>Hysterectomy Rate</th>
<th>Recurrence Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lohle P, et al. JVIR 2008;19:319-26</td>
<td>100</td>
<td>54 months (median)</td>
<td>90%</td>
<td>11%</td>
<td>23%</td>
</tr>
<tr>
<td>Spies J, et al. Obstet Gynecol 2005;106:933-9</td>
<td>200</td>
<td>60 months (minimum)</td>
<td>73% of total</td>
<td>13.7%</td>
<td>20%</td>
</tr>
<tr>
<td>Walker W, et al. BJOG 2006;113:464-468</td>
<td>172</td>
<td>60-72 months</td>
<td>&gt; 80%</td>
<td>5%</td>
<td>16%</td>
</tr>
<tr>
<td>Gabriel-Cox et al. AJOG 2007;196:588.e1-588.e6</td>
<td>562</td>
<td>58 months</td>
<td>80%</td>
<td>19.7%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

*Defined as recurrence of symptoms leading to the need for hysterectomy, myomectomy or repeat UAE greater than 12 months after treatment.
# Myomectomy Recurrence Rates

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>Duration of Follow-up</th>
<th>Hysterectomy Rate</th>
<th>Recurrence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finn et al. AJOG 1950;60:109-116</td>
<td>274</td>
<td>4-8 years</td>
<td>9%+</td>
<td>23%</td>
</tr>
<tr>
<td>Brown et al. AJOG 1967;99:126-129</td>
<td>95</td>
<td>5+ years</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Multiple: 26%</td>
<td>Multiple: 59%</td>
</tr>
<tr>
<td>Candiani, et al. BJOG 1991;98:385-389</td>
<td>622</td>
<td>10 years cumulative</td>
<td></td>
<td>27%</td>
</tr>
<tr>
<td>Acien et al. Fert Steril 1996;65: 41-51</td>
<td>80</td>
<td>10 years cumulative</td>
<td>18%</td>
<td>38%</td>
</tr>
<tr>
<td>N (%) **</td>
<td>3 M</td>
<td>1 Y</td>
<td>2 Y</td>
<td>3 Y</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improved</td>
<td>180 (93)</td>
<td>166 (87)</td>
<td>136 (85)</td>
<td>152 (83)</td>
</tr>
<tr>
<td>Not Improved</td>
<td>9 (5)</td>
<td>10 (5)</td>
<td>8 (5)</td>
<td>7 (4)</td>
</tr>
<tr>
<td>Failed</td>
<td>4 (2)</td>
<td>14 (7)</td>
<td>17 (11)</td>
<td>25 (14)</td>
</tr>
<tr>
<td>Expired</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Missing</td>
<td>7</td>
<td>10</td>
<td>39</td>
<td>17</td>
</tr>
</tbody>
</table>


** Percent of known values, rounded to nearest whole number. All patients followed 5 years.
# UFE Long-Term Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Length of Follow Up</th>
<th>Number of Points Completing Follow Up</th>
<th>Number (%) without Symptoms</th>
<th>Reinterventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spies, et al. <em>Obstet &amp; Gyn</em> November 2005</td>
<td>5 years</td>
<td>182/200</td>
<td>133 (73%)</td>
<td>25 hysterectomies 8 myomectomies 3 repeat UFE 3 died of unrelated diseases</td>
</tr>
<tr>
<td>Spies, et al. <em>JVIR</em> February 2007</td>
<td>3 years</td>
<td>69/102</td>
<td>61 (64%)</td>
<td>7 hysterectomies 1 myomectomy</td>
</tr>
<tr>
<td>Walker, et al. <em>BJOG</em> 2006; 113:464-468</td>
<td>5-7 years</td>
<td>172/258</td>
<td>129 (75%)</td>
<td>9 hysterectomies 6 myomectomies 9 hysteroscopic resections 1 ablation 3 hysteroscopies 1 died in car accident</td>
</tr>
<tr>
<td>Katsumori, et al. <em>AJR</em> March 2006</td>
<td>5 years</td>
<td>80/96</td>
<td>69 (89.5%)</td>
<td>10.5% had add’l gynecologic interventions @5 years</td>
</tr>
<tr>
<td>Dutton, et al. <em>BJOG</em> November 2007</td>
<td>4.6 – 8 years</td>
<td>649 UAE 459 hyst</td>
<td>472 UAE 352 hyst</td>
<td>4.5% add’l UAE 4.9% myomectomy 11.2% hysterectomy</td>
</tr>
<tr>
<td>Goodwin SC, et al. <em>Obstet &amp; Gyn</em> January 2008</td>
<td>3 years</td>
<td>1278 UAE</td>
<td>1093 UAE</td>
<td>1.83% add’l UAE 2.82% myomectomy 9.79% hysterectomy</td>
</tr>
<tr>
<td>Lohle P, et al. <em>JVIR</em> 2008</td>
<td>4.5 – 7.25 years</td>
<td>93 UFE</td>
<td>67 (72%) UFE</td>
<td>8 (31%) add’l UAE 4 (15%) myomectomy 11 (42%) hysterectomy 3 (12%) no improvement</td>
</tr>
<tr>
<td>Publication</td>
<td>Publication</td>
<td>Publish Date</td>
<td>Patients</td>
<td>Bleeding</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------</td>
<td>--------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Spies</td>
<td>JVIR</td>
<td>Feb 2007</td>
<td>102</td>
<td>74%</td>
</tr>
<tr>
<td>REST Investigators</td>
<td>NEJM</td>
<td>Jan 2007</td>
<td>106</td>
<td>N/A</td>
</tr>
<tr>
<td>Siskin</td>
<td>JVIR</td>
<td>August 2006</td>
<td>146</td>
<td>N/A</td>
</tr>
<tr>
<td>Mara</td>
<td>EJoGRB</td>
<td>June 2006</td>
<td>30</td>
<td>N/A</td>
</tr>
<tr>
<td>Smeets / Lohle</td>
<td>CVIR</td>
<td>April 2006</td>
<td>135</td>
<td>79%</td>
</tr>
<tr>
<td>Katsumori</td>
<td>AJR</td>
<td>March 2006</td>
<td>96</td>
<td>N/A</td>
</tr>
<tr>
<td>Wouter WK</td>
<td>CVIR</td>
<td>Jan 2006</td>
<td>156</td>
<td>N/A</td>
</tr>
<tr>
<td>Goodwin</td>
<td>Fertility &amp; Sterility</td>
<td>Jan 2006</td>
<td>149</td>
<td>N/A</td>
</tr>
<tr>
<td>Walker</td>
<td>BJOG</td>
<td>Dec 2005</td>
<td>258</td>
<td>80%</td>
</tr>
<tr>
<td>FIBROID Registry</td>
<td>Ob &amp; Gyn</td>
<td>Nov 2005</td>
<td>1701</td>
<td>N/A</td>
</tr>
<tr>
<td>Spies</td>
<td>Obstetrics &amp; Gynecology</td>
<td>Nov 2005</td>
<td>182</td>
<td>N/A</td>
</tr>
<tr>
<td>FIBROID Registry</td>
<td>Obstetrics &amp; Gynecology</td>
<td>July 2005</td>
<td>3160</td>
<td>N/A</td>
</tr>
<tr>
<td>Razavi</td>
<td>AJR</td>
<td>June 2003</td>
<td>67</td>
<td>92%</td>
</tr>
<tr>
<td>Pinto</td>
<td>Radiology</td>
<td>Feb 2003</td>
<td>40</td>
<td>86%</td>
</tr>
<tr>
<td>Pron</td>
<td>Fertility &amp; Sterility</td>
<td>Jan 2003</td>
<td>555</td>
<td>83%</td>
</tr>
<tr>
<td>Spies</td>
<td>Obstetrics &amp; Gynecology</td>
<td>Nov 2002</td>
<td>400</td>
<td>N/A</td>
</tr>
<tr>
<td>Walker</td>
<td>BJOG</td>
<td>Nov 2002</td>
<td>400</td>
<td>84%</td>
</tr>
<tr>
<td>McLucas</td>
<td>J Am Coll Surg</td>
<td>Jan 2001</td>
<td>167</td>
<td>92%</td>
</tr>
<tr>
<td>Brunerreau</td>
<td>AJR</td>
<td>Nov 2000</td>
<td>58</td>
<td>97%</td>
</tr>
<tr>
<td>Pelage</td>
<td>Radiology</td>
<td>2000</td>
<td>80</td>
<td>90%</td>
</tr>
<tr>
<td>Goodwin</td>
<td>JVIR</td>
<td>1999</td>
<td>60</td>
<td>91%</td>
</tr>
<tr>
<td>Goodwin</td>
<td>JVIR</td>
<td>1997</td>
<td>11</td>
<td>85%</td>
</tr>
</tbody>
</table>
## UFE Benefits Compared to Surgery

<table>
<thead>
<tr>
<th></th>
<th>UFE(^1)</th>
<th>Hysterectomy(^1)</th>
<th>Myomectomy(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay</td>
<td>&lt; 1 day</td>
<td>2.3 days</td>
<td>2.5 days</td>
</tr>
<tr>
<td>Return to work</td>
<td>10.7 days</td>
<td>32.5 days</td>
<td>37 days</td>
</tr>
<tr>
<td>Minor complications(^3)</td>
<td>28.4%</td>
<td>52%</td>
<td>All AEs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>35.6% UFE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>71.7% MYO</td>
</tr>
<tr>
<td>Major complications(^3)</td>
<td>3.9(^1)%</td>
<td>12%</td>
<td>1.7%</td>
</tr>
<tr>
<td></td>
<td>4.0(^2)%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


- Minor complications include Society of Interventional Radiology complication classification levels A & B
- Major complications include Society of Interventional Radiology complication classification levels C or higher
UFE Complications

- Fibroid expulsion: 3-7%
- Vaginal discharge: 0-5%
- Endometritis/Infection: 0-3%
- Ovarian failure: 1-2%
- Contrast, medication allergies: 1%
- Groin site complications: 1%
**Ideal UFE Candidates**

- Most patients with symptomatic fibroids
- Patients with symptomatic fibroids and not pregnant
- Patients wishing to avoid surgery and/or long recovery
- Patients desiring uterine preservation
- Perimenopausal patients
- Poor surgical candidates
  - Medical: anemia, anti-coagulated, obesity, cardiac disease
  - Surgical: extensive adhesive disease
  - Refusing blood products
- Patients who do not desire future fertility
- Patients with hysterectomy/HRT concerns
Contraindications

- Pelvic infection
- Severe contrast allergy
- Arteriovenous shunting
- Coagulopathy
- Renal insufficiency
- Pelvic radiation
- Undiagnosed pelvic mass
- Genital tract malignancy
- Pregnancy
- Size of fibroids
- Adenomyosis
- Desire for future fertility
IR Expectations

Expectations of IR – Patient Work-Up

- Provide patient education and answer questions regarding UFE procedure
- Initiate pre-UFE consult with patient and coordinate workup with OB/Gyn
- Communicate to OB-Gyn if patient is a candidate, and coordinate scheduling of the procedure
- Admit patient into hospital and perform procedure
- Provide complete patient follow-up care and communicate key issues/procedure results with OB-Gyn
- Schedule patient follow-up visits
The IR will manage:

- Catheter site care
- Overnight admission
- Pain control
- Discharge instructions/meds
- Outpatient follow-up
  - 1 week
  - 30 days
  - 3 months
UFE Summary

- UFE is proven effective with durable symptom control
- ~30,000 UFE procedures performed annually in US
- 80% - 95% clinical success
  - Bleeding and bulk-related symptoms
- Clinical studies show equivalent symptom relief compared to surgery with less recovery time and complications
- Minimally invasive; outpatient service for most
- Patients return to normal activity in about 1 week
- Low complication rate
Conclusions

- Long-term studies confirm durability of symptom control in most patients
- Low rates of re-intervention, but does increase with time
- Initial reproductive results appear to favor myomectomy over embolization in first 2 years after treatment
- Additional studies comparing the impacts of myomectomy and embolization on ovarian function and to better assess reproductive outcomes and recurrence rates