Uterine Fibroids: An introduction

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• Co-investigator, Clinical study to evaluate safety of ExAblate Model 2100 System for Symptomatic Uterine Fibroids
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• Co-investigator, FIRSTT trial (Comparing UAE and FUS)

• Co-investigator, Study of environment, lifestyle and fibroids
Objectives

• Discuss the biology, epidemiology, and impact of fibroids
• Describe the clinical presentation and effects on quality of life
• Provide an overview of the medical and minimally invasive fibroids therapies
What are fibroids?

• Benign smooth muscle cell tumor: “leiomyoma”
• Bulky fibrous physiologically active extracellular tissue (collagen): “fibroids”
• Arise from single cell & are monoclonal
  • But, a single uterus can have multiple independent tumors
• Most common reproductive tumor in women
What are fibroids?

- Hormonally dependent
  - Menarche $\rightarrow$ menopause
  - Estrogen, progesterone and aromatase receptors in fibroid tissue
- Chromosomal abnormalities are common (40%)
  - Trisomy 12
  - T(12;14)
  - Deletions of 7q, 3q, 1p
How do leiomyosarcomas differ?

• Rare, fatal tumors with 4 histologic patterns:
  • Nuclear atypia
  • Mitotic activity
  • Necrosis
  • High cellularity

• Fibroid variants may have one of the above but not all
  • Usually benign course
Fibroids grow at different rates

- Fibroids in same uterus grow (or shrink) at different rates
- Range of growth: -89% to +138% in 6 months (median +9%)
- For black women: growth continued at same rate up to menopause
  - For white women: growth rate slowed after age 45

Peddada et al, PNAS, 2008
Fibroid are common

- Symptomatic fibroids: estimated 25%
- Pathology specimens: ~80%
- Ultrasound-screening studies: up to 80% by age 50
- Incidence differs between white and black women
  - Studies of self-reported fibroids: 9 (white) - 34 (Black)/1000 woman-yrs

Public Health Impact of Fibroids

• 400,000 new cases per year\(^1\)

• Myomectomy
  • >30,000 per year in US
  • Direct & indirect costs: $30,206-$39,207\(^2\)

• Hysterectomy
  • 600,000 per year in US
  • 40% for fibroids
  • Direct & indirect costs: $31,559- $42,619\(^2\)
  • Health disparity: black>>white women\(^3,4\)

\(^1\)Hartmann et al, 2006, \(^2\)Carls et al, 2008; \(^3\)Viswanathan, 2007
\(^4\)Eltoukhi et al, 2013
How do women present clinically?

- Menstrual cramps and pain
- Heavy menstrual bleeding & anemia
- Problems with fertility or pregnancy
- Bladder or bowel symptoms
Fibroid size compared to pregnancy weeks
Black women are disproportionately affected

• More symptoms
  • 40% report menstrual pain and cramps
  • 3-fold increased risk of anemia
• 2.4x risk of hysterectomy
• Nearly 7-fold risk of myomectomy
• Higher uterine weights
• More fibroids & larger volume

Fibroids affect quality of life

- Relationship impacts:
  - 14% childcare, 15% friends, 22% partner

- Work:
  - 29% missed work days
  - 24% reported lost potential
  - 27% unable to do part of their job
  - 12% feared losing their job
  - 15% could not travel

Stewart et al, 2013
Fibroids affect quality of life

• Fears about fibroids:
  • 77% growth
  • 53% cancer
  • 25% unable to become pregnant (twice as high in African American women than white)

• Concerns about treatments:
  • 81% invasiveness
  • 64% sexuality

• 49% wanted fertility sparing option (70% v. 30%)

Stewart et al, 2013
Fibroid evaluation

- Pelvic exam
- Ultrasound
- Endometrial biopsy
- Blood counts

- Pelvic MRI
- ?Hysteroscopy
When do we treat fibroids?

• Fibroids that are symptomatic at any age can be treated
  • Imaging will help
• Options: treat symptoms vs. treating fibroids
• Fertility issues:
  • Submucosal fibroids
  • Intramural fibroids >5 cm
  • Treatments that optimize future fertility:
    • MRgFUS
    • Myomectomy
When do we **not** treat fibroids?

- Asymptomatic or an incidental finding
- Rapid growth without symptoms
- Postmenopausal*
Treatment options for bleeding

- NSAIDs
- Tranexamic acid
- Contraceptive hormones (estrogen-progestin or progestin alone)
- Mirena IUD
- Endometrial ablation
Medical options for fibroids and bleeding

- Leuprolide acetate:
  - GnRH agonists/antagonists
  - Controls bleeding
  - Shrinks fibroids

- Ulipristal acetate:
  - Selective progesterone-receptor modulator
  - Controls bleeding in >90% of women
  - Shrinks fibroids
  - Not available for use in US currently
Minimally Invasive Treatments
Uterine Artery Embolization
UAE: how it works

- Catheter placed in common femoral artery
- Travels through anterior internal iliac to uterine arteries
- Position confirmed with angiography
- Embolic agents (polyvinyl alcohol particles)
- Compression on incision to reduce hematoma
UAE: Candidates

- UAE has a more global treatment
- Relative cut-off of 10 cm
- No active genitourinary infection/ malignancy
- No severe vascular disease (limits vessel access)
- No iodine contrast allergy
- Good renal function
- Hysteroscopically resectable SM fibroids
UAE: Details

• 2-3 hour procedure under fluoroscopy
• Overnight stay for pain control
• Incision in groin
UAE: risks

- Amenorrhea: 3% if <40 yrs, 40% if >50 yrs
- Markers of ovarian reserve have shown lower ovarian function after UAE compared with myomectomy
  - Also found with hysterectomy
- Postembolization syndrome: pain, nausea, vomiting, leukocytosis, malaise
Symptom Relief from UAE

• Menorrhagia: 83% improved
• Dysmenorrhea: 77% improved
• Urinary frequency: 86% improved
• 91% satisfaction
• Fibroid volume reduced 42% at 3 months
  • Symptoms unrelated to volume reduction
Pregnancies after UAE

• 164/555 desired fertility (? 35 trying at 1 year)
  • 24 pregnancies
  • 18 live births – 4 preterm
  • 3 abnormal placentations

• 23/102 desired fertility
  • 61% pregnancy rate
  • 2 miscarriages
  • 13 went to term without complication

Pron et al, Obstet Gynecol, 2005; Firouznia et al, AJR, 2009
MRgFUS: how it works

• FDA approved in 2004

• Focused ultrasound beam
  • Temperature highest in focal spot
  • Non-target areas relatively safe

• MRI:
  • Mapping of fibroids & beam guidance
  • Thermal monitoring
  • Treatment effect
MRgFUS: Candidates?

- Few large fibroids
- Accessible by FUS
- Relative cut-off at 10 cm in diameter
- No metal or scars
- Good renal function due to Gadolinium use
MRgFUS: Details

• ~3 hour treatment, possible 2 days in a row
• Done under IV sedation/pain medications and with urinary catheter
• Outpatient (goes home same day)
• Requires minimal pain medication prescriptions
• No incisions/ no radiation
Fibroid before treatment (left image). Treated fibroid (right image).
MRgFUS: Risks

- Skin burns: resolved with procedural changes
- Inflammation of subcutaneous fat and muscle
  - Mainly asymptomatic
- Bowel injury
- Paresthesias:
  - Sonicate 4cm from bony structures
  - Generally spontaneously resolve

Hesley et al. Ultrasound Q, 2008
Symptom relief from MRgFUS

• Symptoms lowest at 3 months
  • Symptom severity score dropped by 50%
  • 91% have symptom relief at 12 months

• Probability of another procedure:
  • The more volume you treat, the better the outcome
  • ~20% at 2 years with 50% treated
  • ~20% at 4 years with unrestricted treatment

Stewart et al. Obstet Gynecol 2007
Fennessy et al. Radiology 2007
MRgFUS: fertility-sparing option

• Observational studies only
• 54 pregnancies
  • 51% delivered at term, 33% miscarried
  • High vaginal delivery rate
  • No distinct patterns of complications
• Success with *in vitro* fertilization after MRgFUS
• Counsel women on the risks that are known and unknown

Rabinovici, Fertil Steril, 2010
Summary

• Fibroids are common and costly
• African-American women are disproportionately affected
• Symptomatic fibroids can be treated, asymptomatic fibroids can be left alone
• There are many alternatives to hysterectomy that are durable and effective
Questions?