Sonography of the Endometrium

Ultrasound of the Endometrium

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Ultrasound of the Endometrium

- Why we worry
- Terminology and Technique
- What is abnormal?
  - Pre-menstrual
  - Post-menstrual
  - HRT
  - Tamoxifen
- Abnormalities seen on TVUS
- Other Diagnostic Modalities
- SIS

Why We Worry?
Endometrial Cancer

- 10% of postmenopausal women will bleed
- 10% of those women will have endometrial cancer (EC)
- 10% EC in women < 50
- EC is the most common GYN malignancy
  - ~39,000 cases/yr USA
  - 4th most common cancer in women (breast > lung > colon), but just 1.5% cancer deaths because of early presentation (bleeding)

Terminology

- Menorrhagia - heavy or prolonged menstrual flow (> 7 days, hypermenorrhea)
- Metrorrhagia - intermenstrual bleeding
- Menometrorrhagia - prolonged uterine bleeding occurring at irregular intervals
- Dysfunctional Uterine Bleeding (DUB) - excessive uterine bleeding with no demonstrable organic, systemic, or iatrogenic cause. It is most frequently due to abnormalities of endocrine origin, particularly anovulation. Diagnosis of exclusion.
- PMB - bleeding that occurs more than 6-12 months after the last menstrual cycle
- AUB (Abnormal Uterine Bleeding) - all of the above

Endometrial Measurement: Technique

“Attention to the little details is the foundation of excellence”

John Wooden

How to Measure the Endometrium

- Transvaginal measurement
  - Empty bladder
  - Also uterus, ovaries, and TAS for fluid/ovaries/masses
- Sagittal plane
- Thickest portion, excluding the hypoechoic inner myometrium
- Double thickness measurement, excluding fluid in the endometrial cavity
- Must visualize the entire endometrium
  - If fibroids obscure, exam is inadequate
  - Will occur 5-10% of the time
  - “Midline echo could not be described as definitely abnormal or normal in 24% of the patients during TVS” (Kazandi 2003)
- If endometrial margins are indistinct (a potential sign of endometrial cancer), exam is inadequate
- Inter and intraobserver reproducibility is good (Epstein 2002)
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How to Measure the Endometrium: Transvaginal

Endometrial polyp seen much better at TVS

Goldstein R. JUM 20:2001

How to Measure the Endometrium: Exclude the hypoechoic inner myometrium (♂) in PMB

How to Measure the Endometrium: If endometrial fluid is present, measure each wall separately and sum; don’t include the central fluid

How to Measure the Endometrium: Sweep the entire endometrium

Stage I AdCa not seen on initial image

How to Measure the Endometrium: Visualize the entire endometrium

Fibroids Obscuring Stage IIb Endometrial Cancer

How to Measure the Endometrium: Don’t accept indistinct endometrial margins

Grade 2 adenocarcinoma
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What is Abnormal Endometrium?

Scenario I: Premenopausal

- Appearance changes throughout the cycle
- Follicular = proliferative phase
- Luteal = secretory phase
- Upper normal in late secretory phase is listed between 12-16 mm. I use 15 mm, but realize this is a “soft” threshold

Endometrial Appearance: Immediately post-menses or post-menopausal

20 yo on OCP day 4

Endometrial Appearance: Proliferative (Follicular)

Day #07

Endometrial Appearance: Peri-ovulatory

Day #14

Day #17

Endometrial Appearance: LateSecretory (Luteal)
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Endometrial Appearance:
ULN 15 mm is Not a Perfect Threshold

2.5 cm endometrium in 29 yo asymptomatic patient on day 27:
Schedule early in the cycle

What is an Abnormal Endometrium?
Scenario II: PMB

- Double thickness > 5 mm
  - (Smith-Bindman JAMA 1998 and Goldstein JUM 2001)
  - Risk of endometrial cancer with an endometrial thickness of > 5 mm is ~0.5-1% (Timmerman 2003)
  - 4 or 5 mm threshold is not perfect! (Gupta 2002)

- Focal endometrial abnormality
- Indistinct appearance of the endometrial lining
- Non-diagnostic (fibroids, etc)
  - 5-10% of cases

An abnormal test does not mean the woman has cancer!!!
- Obstetrical sonography: the best way to terrify a pregnant woman (Filly JUM 2000)
- Polyps, hyperplasia, fibroids, ... (and most EC is readily treatable)
- Most common cause of PMB is atrophy (~60%), but cancer (including complex hyperplasia with atypia) must be ruled out
- "Up to 80% of women with PMB and ET > 5 mm have endometrial pathology" (Epstein 2001)

55 yo on unopposed estrogen for 5 years p menopause (per patient wishes)

16 mm endometrium shown to be benign at path obtained during hysteroscopy

What is an Abnormal Endometrium?
Scenario III: PMB ON HRT

- Problem going away!
- When to scan?
  - TVUS 4-5 days after completion of cyclic bleeding in women on sequential HRT
  - TVUS at any time in women on continuous HRT
- Keep 5 mm threshold (no data to widely quoted 8 mm #)- same sensitivity but accept more FP

What is an Abnormal Endometrium?
Scenario IV: PM but NOT Bleeding

- Should we offer additional investigations to asymptomatic women with an increased endometrial thickness on ultrasound scan?

16 mm endometrium shown to be benign at path obtained during hysteroscopy
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What is an Abnormal Endometrium?

Scenario IV: PM but NOT Bleeding
- Meta-analysis: > 11 mm biopsy (cancer risk 6.7%), whereas <= 11 mm no biopsy
  - Smith-Bindman Ultrasound Obstet Gynecol 2004
- Theoretically, a screening program based upon this would have a PTR of 0.25% (4/1000)
  - Is this true in the real world? Even if it was, would it result in improved endometrial cancer survival rates? Or, as in many well-meaning screening programs, would we see most from surgery with no benefit in women who would die with, rather than of, EC?
- ‘No consensus on the usefulness of regular scans in postmenopausal women or cut-off that should trigger further investigations. In the absence of a consensus the onus should be on the proponents of interventions to justify the benefits to their patients and peers… Primum non nocere!”
  - Jurkovic Ultrasound Obstet Gynecol 2005
- But, our Gyn-Onc experts recommend further tissue work-up if an endometrial thickness > 11 mm is picked up incidentally

Meta-analysis: > 11 mm biopsy (cancer risk 6.7%), whereas <= 11 mm no biopsy

What is an Abnormal Endometrium?

Scenario V: Tamoxifen
- Tamoxifen (SERM) halves the risk of breast cancer recurrence
- Tamoxifen stimulates the endometrium
  - Long-term use of tamoxifen increases the risk of endometrial cancer 7x+5 years
  - Strong overall benefit to tamoxifen

But, our Gyn-Onc experts recommend further tissue work-up if an endometrial thickness > 11 mm is picked up incidentally

What is an Abnormal Endometrium?

Numeric Summary
- Postmenopausal, bleeding: > 5 mm
- Postmenopausal, bleeding and on HRT: > 5 mm*
- Tamoxifen: > 5 mm*
- Postmenopausal, NOT bleeding: > 11 mm*
- Premenopausal: > 15 mm *

* lots of “discussion” about these values!


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TVUS: Atrophy

~60% of PMB is atrophy

Tamoxifen Polyp

March 2002

June 2003

Path after TAH • Benign polyps
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TVUS: Polyps

TVUS: Polyps

TVUS: Fibroids

TVUS: Endometrial Cancer

Note submucosal location

65 yo with intermittent spotting:

Grade I adenocarcinoma within polyp

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 Alternative Procedures: Hysterosalpingogram (HSG)

- Poor for the endometrium: essentially obsolete except for tubal patency
- Hysteroscopy revealed synchieae, polyps, or myomas in 40% of patients with normal HSGs
- 1 in 3 women diagnosed as having an intrauterine filling defect by HSG will have a normal cavity by hysteroscopy
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**Alternative Procedures: Dilation and Curettage (D&C)**
- Decreasing popularity with US, EMB, and hysteroscopy
- Only samples 10-20% of the endometrial cavity
  - OK for endometrial cancer (but EMB < D&C)
  - Not good for polyps or other focally growing lesions
  - D&C misses the diagnosis in 10-25% of women

**Alternative Procedures: Endometrial Biopsy**
- Thin suction catheter used to sample endometrial lining in office
- Accuracy for EC is ~95%
  - If + EMB in PMB, no need for further imaging
  - 10% who had a negative EMB turned out to have cancer or complex hyperplasia
- Only samples ~15% of endometrial surface
- Poor for polyps: sensitivity of 4% (EMB) vs 100% (SIS)
- More painful than SIS

**Alternative Procedures: Hysteroscopy**
- Office (10% failure) vs. OR
- Endometrial cavity filled with fluid, usually dextran
- Hysteroscopy with directed biopsy offers the best chance of making an accurate diagnosis but is costly and invasive
- "EMB coupled with SIS is a reliable office tool for identifying patients who should be considered for surgical intervention" (O'Connell 1998)
- SIS is equivalent in diagnostic accuracy to HS (multiple studies)

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**Saline Infusion Sonohysterography (SIS)**
- AKA sonohysterography, hysterosonography, transvaginal sonography with fluid contrast augmentation, saline infused sonography
- From the: Latin sonus -> sound
  Greek υστέρα -> hystera -> womb
  Greek γράφος -> graphy
  -> writing

**SIS Overview**
- 68 citations found when searching for "sonohysterography" from 2000 through April 2006
- Our lab has averaged 72/year for the past 6 years
- Not a difficult study to perform!
  - No difference in accuracy between NP, PGY2, PGY4 and fellows (Parker 2004)
  - "Routine use of this method even in non-expert hands implies a low number of undiagnosed lesions" (Dueholm 2001)
  - Always perform conventional TVS first
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**Is SIS Overkill? Is TVUS Alone Good Enough?**

- The diagnostic potential of TVS in experienced hands has been found to be in line with that of hysteroscopy, but not when less experienced operators performed the examination (Emanuel 1995, Towbin 1996, Bernard 1997)
- TVS with Doppler and SIS had similar performance for diagnosing polyps (Alcazar 2004)

**Overwhelming bulk of the literature says TVUS alone is NOT adequate**
- "TVS alone left 1 in 5 polyps undiagnosed in referred patients for abnormal bleeding" (Dueholm 2001)
- "Accuracy of [SIS] was significantly better than [TVS] considering all intrauterine pathologies" (Ragni 2005)
- "Midline echo could not be described as definitely abnormal or normal in 24% of the patients during TVS" (Kazandi 2003)
- "The added information provided by [SIS] resulted in improved diagnostic confidence for most parameters. Agreement was markedly improved for the diagnosis and location of submucous myomas and focal endometrial lesions" (Becker 2002)
- "In patients presenting with abnormal vaginal bleeding, a SIS may be warranted despite a normal TVS" (Laifer-Narin, 2002)
- "29.7% of the women with a normal TVS had an abnormal SIS" (Neele 2000)

**SIS Indications**

- Abnormal bleeding in premenopausal or postmenopausal patients
- Evaluation of an endometrium that is thickened, irregular, immeasurable, or poorly defined on conventional TVUS
- In cases where ET >5 mm, but sampling reveals atrophic endometrium (discordance)
- Irregular-appearing endometrium with TVUS in women using tamoxifen
- Differentiate between sessile and pedunculated masses of the endometrium
- Presurgical evaluation of intracavitary fibroids
- Infertility evaluation
- RPOC, C-section scar, ...

**SIS Indications: Discordance**

48 yo c irregular bleeding. TVUS showed 17 mm stripe path (EMB) → normal endometrium

SIS → 3.8 cm polyp
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SIS: Primary Goal

Focal (surgical) vs. diffuse (medical) disease
One cannot reliably distinguish malignant from benign disease

“SIS is effective in the assessment of uterine bleeding because of its ability to distinguish patients without any intracavitary lesion (who just need medical treatment) from those who need further (surgical) evaluation” (Bernard 2001)

Laifer-Narin 1999 provides a counterpoint
We're pretty good on fibroids vs polyps, and most polyps are benign (but still usually come out)

SIS: Technique

Preparation:
“A pint of sweat will save a gallon of blood”
General George Patton

- Schedule between day 4 and day 7 (2-5 days postmenstrual stops)
- NSAID 30’ before
- Psychological “warmth”
- Other
  - PID/doxy
  - IUD
  - SBE prophylaxis

...Sonohysterography: Lessons in Technique. AJR 2006;186(1):24

Why SIS during Days 4 to 7?

- Precludes scanning during pregnancy
- Fewer ovarian cysts
  - 1. women in the reproductive years should be scheduled for evaluation of the ovaries immediately after the menstrual flow ends, roughly on days 5 to 9 of their cycle...
  - Goldstein and Timor-Tritsch, JUM 2005; 24:255
- Avoid endometrial false positives that occur when scanning in the secretory/luteal phases
- nb
  - In women with AUB, scan at any point in the cycle
  - Use the catheter tip to distinguish clot from real pathology

SIS: Equipment

- Routine
  - Cramping (wait 30’ for NSAIDs)
  - Spotting
- Rare
  - Infection <1% (? AB with hydrosalpinx on TVUS)
    - 2/2378 (0.01%) UTI (deKroon 2003)
    - Endometritis <1%
      (Bonnamy 2000)
  - 3/2278 vasovagal
    (deKroon 2003)
  - ??? Endometriosis
  - Perforation
  - ??? Upstaging (seeding) endometrial cancer

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Equipment: The Catheter
- Which one? It’s the operator, not the equipment
- 6 catheters in 610 women
  - No real differences between systems, but Foleycath most difficult to use and Goldstein best tolerated by patients
- Embryo transfer catheter or 5 Fr dilator over 0.038” glide

How to perform an SIS: Choose the Correct Speculum
- Specula come in two basic shapes and are made of metal or plastic
- Both Pederson and Groves specula are available in small, medium, and large sizes
- Start with medium Pederson
- Small Pederson for small introitus (virgins or elderly)
- Medium Groves for women s/p NSVD or obese
- Large Groves for multip, very obese and/or vaginal prolapse

How to perform an SIS: Insert the Speculum Correctly
- Lubricate and warm the speculum with warm water for comfort (gel OK, especially in PMF with atrophic vagina)
- Ease insertion:
  - Patient Valsalva or
  - Depress perineal body
- Insert with 45° angle and oblique; avoid sensitive anterior wall/urethra

Insert the Speculum Correctly
Spend your time here. Get this sight picture. This is the most difficult part of the exam!
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How to perform an SIS:
Pass the Catheter

- The 2nd most difficult part of the exam
- Patient history
  - 80 yo G0P0 versus 40 yo with h/o NSVD x 8
- Options for stenotic cervix
  - Sound
  - Specialized catheter
  - 5 Fr dilator over 0.038" glide
  - Tenaculum
    - Apply @ noon, not 3 or 9 o'clock
    - Quit

How to perform an SIS

- Don’t jab fundal endometrium upon cath insertion
- Slowly distend balloon (saline, not air!); minimize volume
- Infuse saline slowly into endometrial cavity; minimize volume

Pull out Imaging

Try Catheter in Cervical Canal

- Why?
  - Less pain
  - Half the volume
  - Successful exam in the setting of a very stenotic cervix

SIS Failures

- 7% failure rate
  - 13.5% failure in postmenopausal vs. 5.2% in premenopausal (P < 0.01)
  - Meta-analysis 278 procedures: de Kroon 2003
- Catheter choice
  - Failure listed as backflow problem but not using occlusive balloon, not using guide wire for stenotic cervix,
    ...
- Other equipment
  - Sound, tenaculum
- Skill, training and determination

[Table showing SIS Failures]
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SIS False Positives & Problems

- Air bubbles (air in balloon)
- Balloon obscuring LUS
- "Small irregularities caused by blood clots or endometrial protrusions were frequently misinterpreted as polyps" (Kazandi 2003)
  - Use your catheter to move stuff
- Mechanical shearing of the endometrium from overzealous placement of the catheter
- Poor timing in menstrual cycle

SIS False Positives & Problems: Air Bubbles

SIS False Positives & Problems: Balloon Obscuring LUS

SIS False Positives & Problems: Blood Clots Mimicking Focal Mass

SIS False Positives & Problems: Mechanical Shearing of the Endometrium

Don’t confuse for a polyp
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**SIS Technology: Colour Doppler & Focal Lesions**
- Polyps typically contain a single feeding vessel
- Fibroids usually have several vessels arising from the inner myometrium
- Broad overlap; not pathognomonic

**SIS Technology: 3D**
- Nice tool if available
  - Speeds exam
  - Multiplanar depiction
  - Image quality of 3D probes now reasonable
- If N/A, use CINE sweep

**Fleischer JUM 2003**

**SIS Technology: 3D**
- Polyp #2 missed with initial 2D scan

**Ledwidge RSNA 2003**

**SIS: Endometrial Polyps**
- Most common endometrial focal lesion
- 30% of PMB
- Typically well-defined, homogeneous, hyperechoic with narrow base of attachment
- Well-defined vascular pedicle typical, but not a reliable indicator of a polyp
- Less commonly, broad base, cystic components, heterogeneous
- Polyps usually come out
  - Treat bleeding
  - Can’t exclude hyperplasia, CIS, focal cancer
  - SIS provides accurate size, location and #, which helps increase success rate of HS resection

**Cooperberg PL. RSNA CC 2002:39-46**

**SIS: Endometrial Polyp**

52 yo with abnormal uterine bleeding; path multiple polyps

**SIS: Endometrial Polyp**

Final path Grade I adenocarcinoma within polyp

Does this image look that different from the previous patient?!

Theme:
Focal masses are suspicious- we cannot perform tissue characterization
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SIS: Endometrial Polyp

- SIS: Endometrial Polyps
- 2nd Polyp not seen until Balloon Deflation

SIS: Fibroids

- 77% prevalence (if you look hard enough at path)
- Symptomatic in about 25%
- Usually associated with DUB, but account for 10% PMB

- European S. of Hysteroscopy Classification
  - Type 0: Entirely within cavity (pedunculated)
  - Type I: > 50% projecting into cavity
  - Type II: Intracavitary extension of <= 50% volume
  - HSG resection possible if > 50% of volume projects into cavity

- “SIS is an important adjunct to TVS in symptomatic women with known or suspected myomas, particularly before medical or surgical therapy” (Becker JUM 2002)

SIS: Fibroids

- Appearance at SIS
  - Broad based, hypoechoic
  - More heterogeneous than polyps
  - Thin rim of encompassing endometrium is highly suggestive (but not always present) of submucosal origin
  - Can be difficult to distinguish pedunculated fibroids and even more typical fibroids from polyps

O’Neill M. RCNA 2003;(41):781
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SIS: Fibroids

SIS: Endometrial Hyperplasia
- 6% of PMB
- Spectrum: simple EH s atypia → severe atypia
- Severe atypia has 20% risk of developing into cancer, while lesser degrees of atypia have very little malignant risk
- Risk factors: obesity & unopposed estrogen, HTN, DM, nulliparity
- Classically diffuse, but focal forms are difficult to distinguish from polyps
- Look at interface between base of polyp/focal EH: if distorted or poorly visualized, risk of more aggressive process increases

SIS: Endometrial Hyperplasia

53 yo with abnormal vaginal bleeding; path: simple endometrial hyperplasia

54 yo with menorrhagia; path: complex endometrial hyperplasia without atypia

SIS: Endometrial Hyperplasia

Endometrial hyperplasia with mild atypia
O’Neill M. RCNA 2003;(41):781

SIS: Endometrial Cancer
- How much you see depends on practice patterns. If patients go to EMB first, you will not see many cases at SIS
- Most common gyn cancer, 4th most common cancer in women
- Wide variety of presentations
  - Large, broad-based (up to most of lining), heterogeneous lesions are worrisome
  - Look at base of attachment for irregularity
  - Incomplete distension has an OR ~7
**Sonography of the Endometrium**

**SIS: Endometrial Cancer**

- **Endometrial carcinoma presenting with malignant hematometra**
  - Cooperberg PL. RSNA CC 2002:39-46

**SIS: Endometrial Cancer**

- **72 yo with PMB → invasive endometrial cancer**
  - Note highly irregular endometrial/myometrial interface
  - O’Neill M. RSNA 2003;(41):781

**SIS: Endometrial Cancer**

- **Incomplete Distension**
  - "The risk of malignancy was increased seven fold (OR = 7.3) in women with distension difficulties at [SIS], and 2/3 of women with a poorly distensible uterine cavity had a malignant diagnosis" (Epstein 2001)
  - Make sure you use good technique, e.g. no leak

**SIS: Endometrial Cancer**

- **71 yo c PMB. Blind EMB before SIS negative;**
  - path focus of papillary serous carcinoma of the endometrium arising within polyp.

**Theme:** Focal masses are suspicious—we cannot perform tissue characterization.
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**SIS Primary Goal: Focal vs. Diffuse**
- We cannot reliably make tissue diagnoses!

**Misc: SIS Tamoxifen**
- SIS may avoid further intervention in 14% of women on tamoxifen who have ET > 8 mm by showing normal endometrium or endometrial cysts (Hann 2001)
- SIS much better than EMB for finding polyps in the tamoxifen population (100% sensitivity vs. 4%) (Hann 2003)
- Vast majority of tamoxifen associated polyps are benign, but some say they should all come out
- Literature is confusing and contradictory on the role of SIS in this population, but most agree that SIS has no role in asymptomatic patients on tamoxifen

**Misc: SIS Infertility**
- Many incorporate SHG/SIS as 1st line screening for uterine evaluation before embryo transfer for IVF, ovum donation, and IVF-surrogacy
- ~20% of younger IVF patients and ~40% of advanced reproductive aged women undergoing ovum donation have intrauterine pathology
- Better than TVS/HSG for evaluation of recurrent abortion

**Misc: SIS Infertility Adhesions**
- Intrauterine adhesions in a 33 yo woman undergoing fertility workup with a history of 2 dilation and curettage procedures

**Misc: SIS Infertility Tubal Anatomy**
- Even though SIS is unequivocally better than HSG for the endometrial cavity, HSG is still the gold standard for the tubes
- Many studies using various synthetic "bubble" agents to evaluate tubal patency
- Air-sonohysterography was 86% sensitive and 77% specific when compared to a gold standard (115 women)
  - "comfortable, simple, and inexpensive first line of tubal patency investigation" (Zienty 2000)

**Misc: SIS Intervention**
- 5 Fr echogenic loop snare passed through 12-Fr intrauterine access catheter with a 3 ml balloon
  - Feasible, cheaper than HS, and deserves further study (Lindheim 2003)
- Not trivial: "SH-EMB cannot replace EMB by HSC", in a trial of 105 patients with irregular uterine bleeding (Metzger 2004)
- Many other specialty, especially operative, applications being investigated
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SIS vs. Other Standards

- Sensitivity, specificity, and predictive value evaluated in multiple studies
- Much better than TVUS in all ways; better than EMB and D&C at detecting focal lesions
- “SIS is as good as diagnostic hysteroscopy under general anesthesia at detecting focal lesions in the uterine cavity. It is better tolerated [than office hysteroscopy], and cheaper.” (Epstein 2001)
- Neither hysteroscopy nor SIS can reliably discriminate between benign or malignant focal lesions, though distension difficulties should raise a suspicion of malignancy

SIS versus Hysteroscopy (HS)

- “Although hysteroscopy has been the gold standard, SIS has undeniable advantages in terms of time, cost, availability, convenience, risk of anesthesia and perforation and the additional information provided regarding myometrium and adnexa.” (Pasrija 2004)
- “Routine use of SIS instead of hysteroscopy in the primary investigation of patients with bleeding disorders would potentially lead to 2 of 3 hysteroscopies being avoided” (Dueholm 2001)
- Randomized controlled series has shown that SIS is better tolerated, required less medical intervention, and provided significant cost-savings when compared with ambulatory office hysteroscopy (Bernard 2001, O’Connell 1998)

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Overview
- Technique
- Examples
  - Polyps
  - Fibroids
  - Hyperplasia
  - Cancer
  - Tamoxifen
  - Infertility
  - RPOC
- Intervention

Summary- “Take Home”

- How to measure ET at TVS
  - <= 5 mm ET “reliably” excludes endometrial cancer
  - > 11 mm ET in asymptomatic postmenopausal → EMB (?!)
- SIS easy to perform, has short learning curve and is a valuable tool; primary goal is focal (surgical) vs. diffuse (medical) disease
- Tamoxifen controversial
  - No screen ax with TVS or SIS
- Problem hopefully going away (same with HRT)

Thank you!

- Art Fleischer & Heidi Shappell. JUM 22(2003):601-604
- Steve Lindheim, personal collection