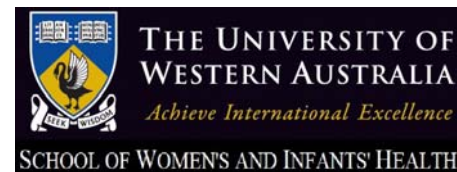


# Endometrial cancer: What we do not know

Y Leung

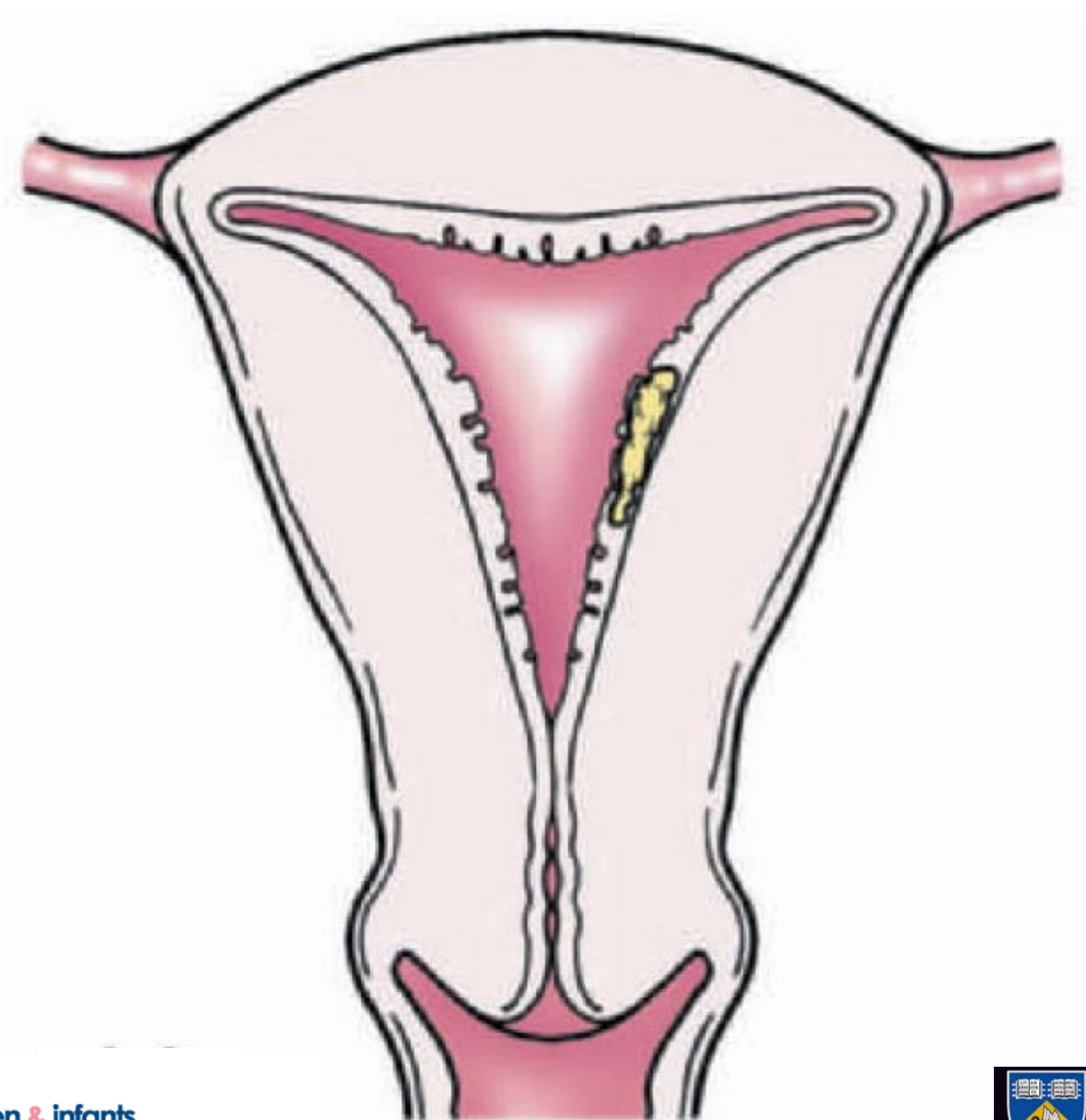
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# Disclosures

- WIRF

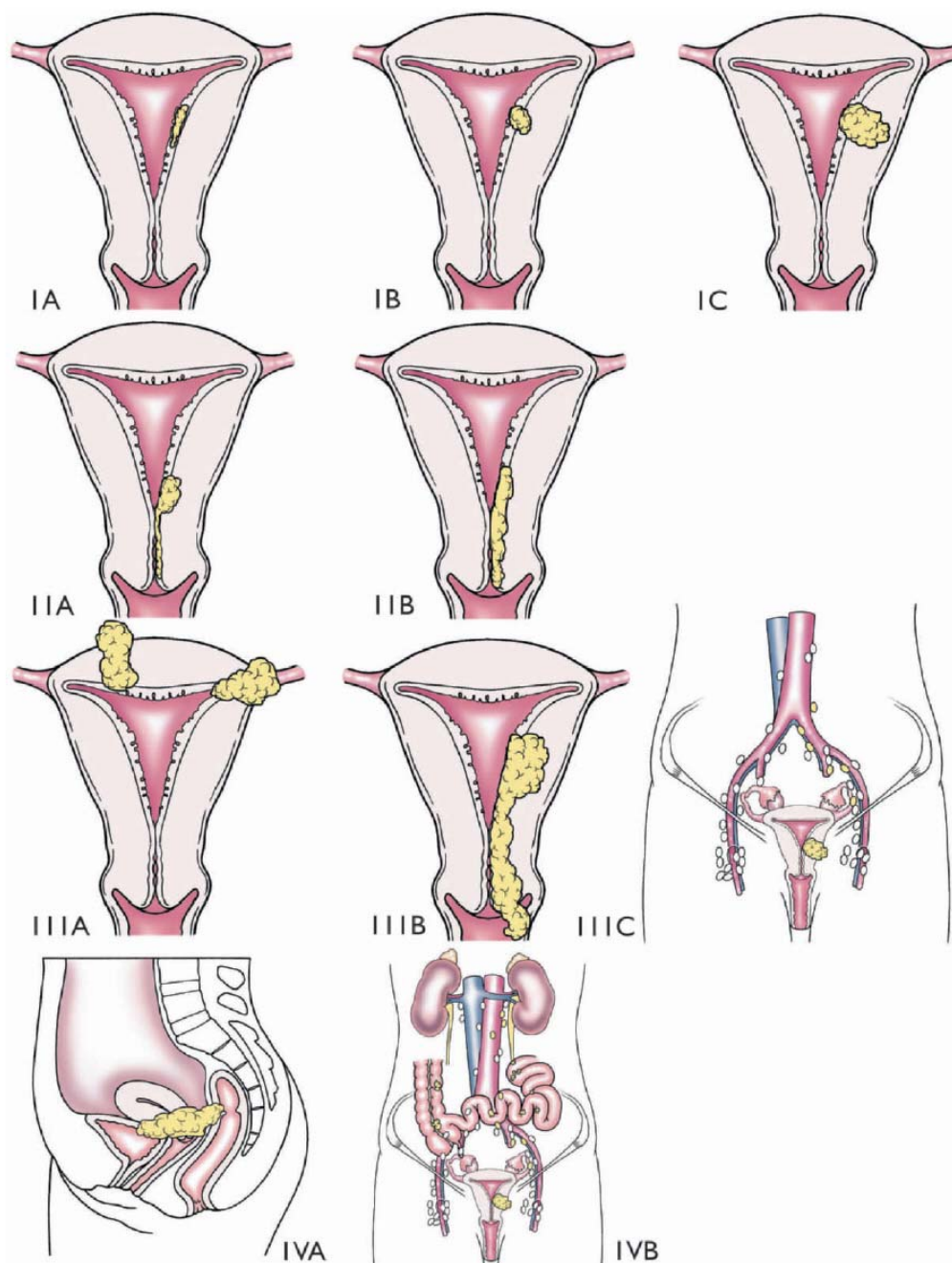


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# What we do not know

- Molecular Biology and all that weird stuff
- Management issues
  - HystBSO and LND
  - Adjuvant therapy
- Followup

# What we do not know

- Stimulate you to ask questions...



THE SIGNS OF TWO MAIN PATHOGENETIC TYPES OF ENDOMETRIAL CARCINOMA<sup>a</sup>

Sign	Pathogenetic types	
	I	II
Menstrual function	Medical history of anovulatory uterine bleeding	No disturbances
Reproductive function	Decreased, frequent infertility	No disturbances
Onset of menopause	Often after the age of 50	Often under the age of 50
Type of colpocytologic reaction in the postmenopause	Estrogenic	Atrophic or transitional
Ovarian status	Hyperplasia of theca tissue Stein-Leventhal syndrome Feminizing tumors	Fibrosis
Endometrial background or results of previous curettage	Hyperplastic processes	Atrophy
State of myometrium	Myoma, internal endometriosis	No changes
Obesity	Present	Absent
Hyperlipidemia	Present	Absent
Diabetes mellitus	Present	Absent
Hypertension	Associated with obesity and/or diabetes mellitus	Absent or not associated with obesity and diabetes mellitus

<sup>a</sup> Peculiarities of the tumor (degree of differentiation, depth of invasion, etc.) have not been taken into account when the pathogenetic type of the disease was determined.

INFLUENCE OF PATHOGENETIC TYPE OF THE DISEASE ON TUMOR PECULIARITIES

Tumor peculiarity	Pathogenetic type	
	I	II
Duration of symptoms	Usually long duration	Usually short duration
Degree of tumor differentiation	Highly or moderately differentiated (more frequent G <sub>1</sub> or G <sub>2</sub> )	Poorly differentiated (more frequent G <sub>3</sub> )
Depth of invasion in the myometrium	Frequent prevalence of superficial invasion	Frequent prevalence of deep invasion
Potentiality for lymphogenic metastatic spread	Not high	High
Sensitivity to progestogens	High	Not high
Primary multiple tumors	Ovaries, breast, colon	Not characteristic
Prognosis	Favorable	Doubtful

JAN V. BOKHMAN GYNECOLOGIC ONCOLOGY 15, 10-17 (1983)

**Table 1.** Genetic Differences Between Cancers With and Without Endometrioid Histology

Gene	Alteration	Endometrioid (type 1; %)	Nonendometrioid (type 2; %)
<i>p53</i>	Inactivating mutation	5-10	80-90
<i>PTEN</i>	Loss of function through deletion and/or mutation	55	11
<i>K-ras</i>	Mutational activation	13-26	0-10
<i>β-catenin (CTNNB1)</i>	Gain of function mutation	25-38	Rare
<i>MLH1</i>	Epigenetic silencing causes microsatellite instability	17	5

## Molecular and Pathologic Aspects of Endometrial Carcinogenesis

*Jonathan L. Hecht and George L. Mutter*

*J Clin Oncol 24:4783-4791.*

# Histological

- MELF – microcystic elongated and fragmented pattern – more likely to be associated with LVSI

Pathology (August 2009) **41(5)**, pp. 454–459

# Question...

- Should the primary management of all subtypes of endometrial cancer be the same?
- Can adjuvant therapy be individualized?

# Endometrioid cancer

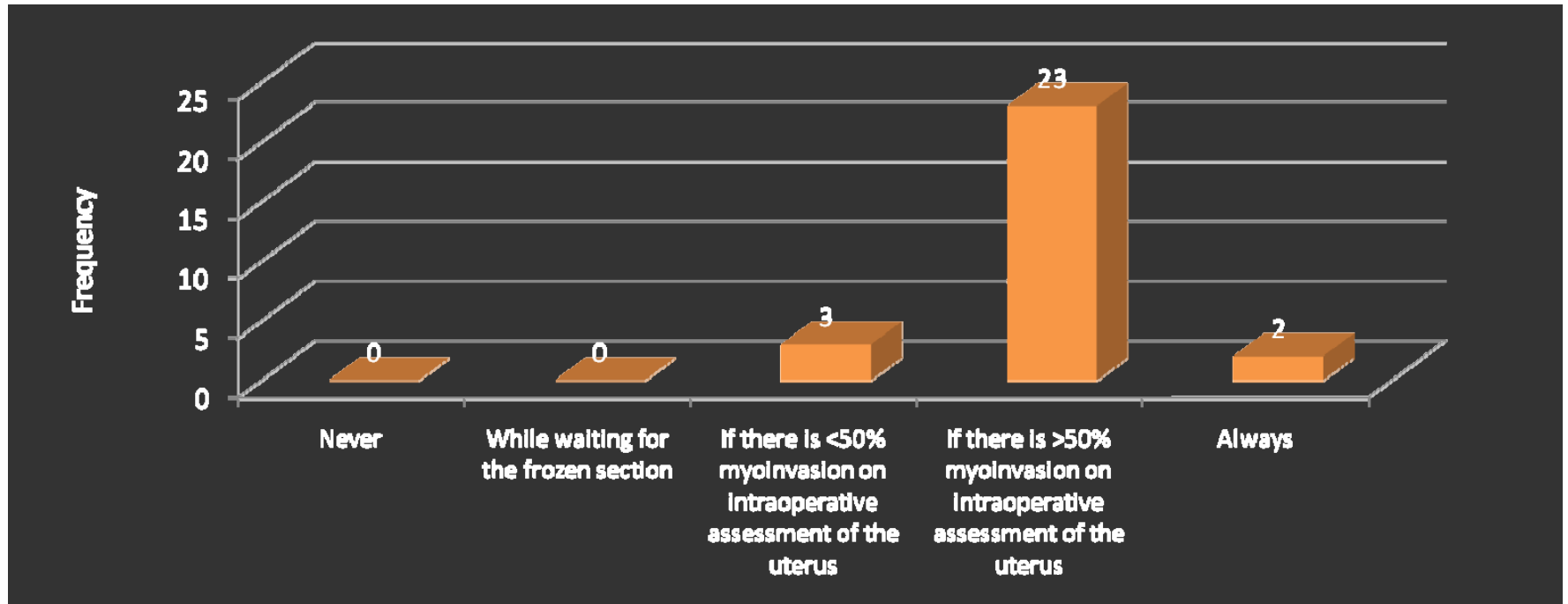
In your practice, you see a fit, non-obese 60 year old with a grade 1 endometrioid adenocarcinoma of the uterus with a negative metastatic workup.

At primary surgery for hysterectomy and BSO, you would perform a pelvic lymphadenectomy:

1. Never
2. While waiting for the intraoperative assessment (IOA)
3. If there is <50% myoinvasion on IOA
4. If there is >50% myoinvasion on IOA
5. Always

# Results – Endometrioid cancer

In your practice, you see a fit, non-obese 60 year old with a grade 1 endometrioid adenocarcinoma of the uterus with a negative metastatic workup. At primary surgery for hysterectomy and BSO, you would perform a pelvic lymphadenectomy:



# Endometrioid cancer

In your practice, you see a fit, non-obese 60 year old post hysterectomy and BSO with a grade 1 endometrioid adenocarcinoma of the uterus with a negative metastatic workup.

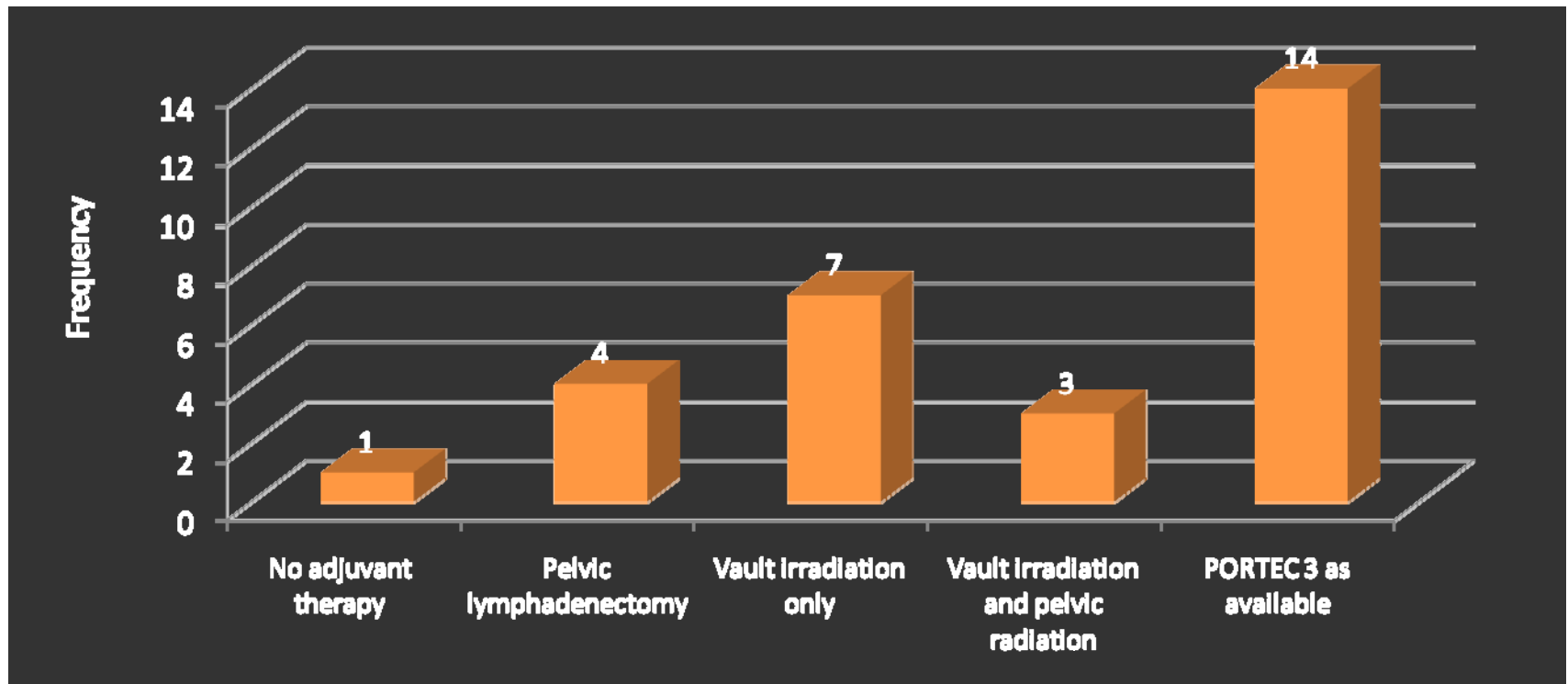
The pathologist reports myoinvasion to 9mm out of 20mm AND cervical stromal involvement.

She did not have a lymphadenectomy. Would you offer:

1. No adjuvant therapy
2. Pelvic lymphadenectomy
3. Vault brachytherapy
4. Vault brachytherapy and pelvic radiation
5. Chemoradiation

# Results – Endometrioid cancer

In your practice, you see a fit, non-obese 60 year old post hysterectomy and BSO with a grade 1 endometrioid adenocarcinoma of the uterus with a negative metastatic workup. The pathologist reports myoinvasion to 9mm out of 20mm AND cervical stromal involvement. She did not have a lymphadenectomy. Would you offer:



# Endometrioid cancer

In your practice, you see a fit, non-obese 60 year old post hysterectomy and BSO with a grade 3 endometrioid adenocarcinoma of the uterus with a negative metastatic workup.

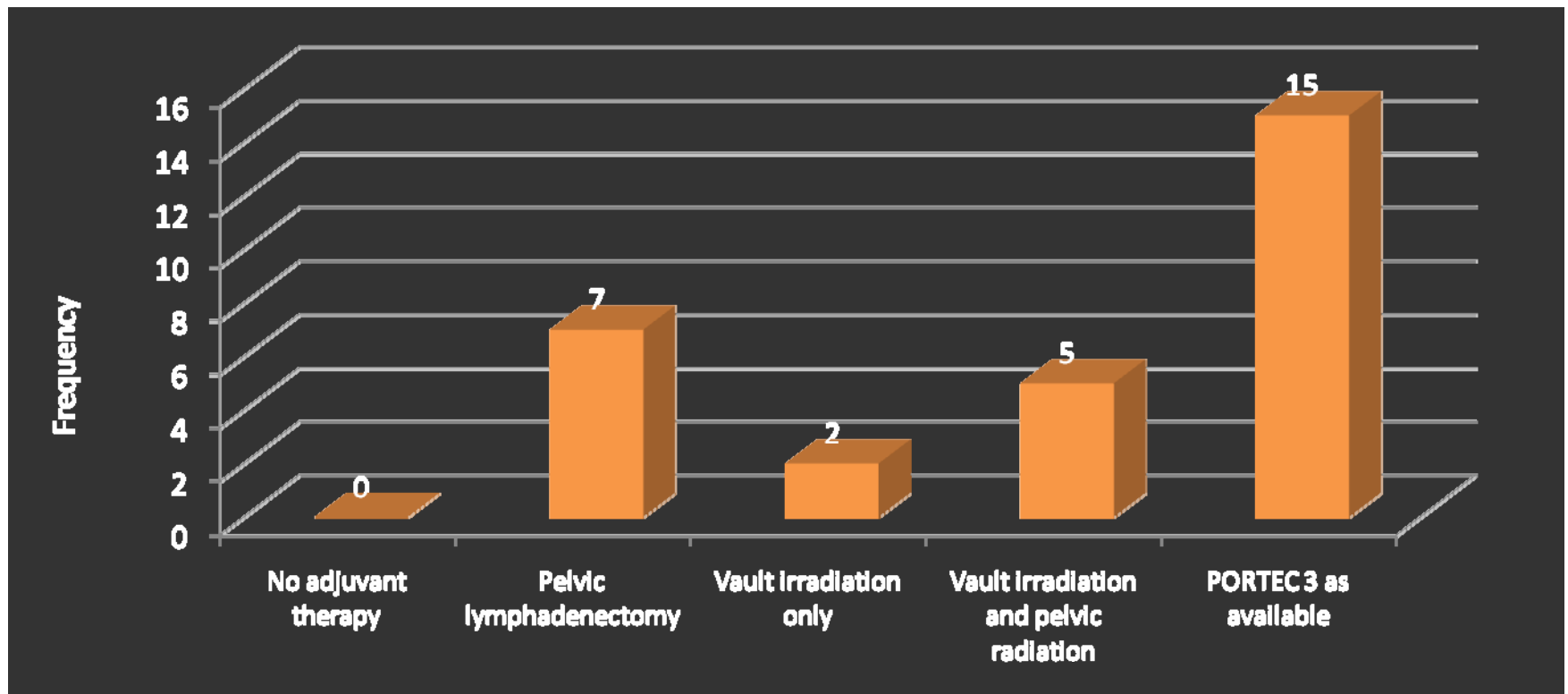
The pathologist reports myoinvasion to 9mm out of 20mm.

She did not have a lymphadenectomy. Would you offer:

1. No adjuvant therapy
2. Pelvic lymphadenectomy
3. Vault brachytherapy
4. Vault brachytherapy and pelvic radiation
5. Chemoradiation

# Results – Endometrioid cancer

In your practice, you see a fit, non-obese 60 year old post hysterectomy and BSO with a grade 3 endometrioid adenocarcinoma of the uterus with a negative metastatic workup. The pathologist reports myoinvasion to 9mm out of 20mm. She did not have a lymphadenectomy. Would you offer:



# Question

- Consensus on post-operative management?

# Followup

- Reasons
  - Research
  - Detect disease early and cure
  - Patient demand
  - Physician demand
  - Target higher risk of recurrence
    - Adjuvant therapy does not affect OS
    - Low risk patients with vaginal recurrence can be salvaged

# Follow-up

- Recurrence rate
  - 13% overall
    - 41 – 100% symptomatic, 38 – 86% distant
  - 3% in low risk
    - Fung-Kee-Fung et al. Gynecol Oncol 2006; 101: 520
- Salvage rate
  - 73% in vaginal
  - 8% in distant
    - Creutzberg et al. Gynecol Oncol 2003; 89: 201 - 209

# Follow-up

- How to follow up
  - Examination (Detection rate 5 – 33%)
  - Cytology (Detection rate 0 – 4%)
  - Imaging/CA 125 (Detection rate 0 – 21%)
    - Smith CJ, Heeren M, Nicklin JL, et al. *Gynecol Oncol* 2007;107:124–9.
    - Fung-Kee-Fung M, Dodge J, Elit L, et al. *Gynecol Oncol* 2006;101:520–9.
    - Sartori E, Pasinetti B, Chiudinelli F, et al. *Int J Gynecol Cancer*. 2010;20:985-92.

**TABLE 1****Sensitivity/detection rate of the methods that were used to detect recurrence in patients at routine visits after treatment**

<b>Method of detection</b>	<b>Type of cancer, %</b>		
	<b>Endometrial</b>	<b>Ovarian</b>	<b>Cervical</b>
Symptoms	41-83	—	46-95
Physical examination	35-68	15-78	29-75
Cytologic evidence	0-7	—	0-17
Chest radiograph	0-20	—	20-47
Cancer antigen 125 level	15	62-74	—
Computed tomography scan	0-20	40-93	0-45 <sup>a</sup>
Positron emission test–computed tomography scan	100 <sup>a</sup>	45-100	86

<sup>a</sup> Limited data.*Salani. Surveillance for gynecologic cancers. Am J Obstet Gynecol 2011.*

# Follow-up

- Intensity/Interval
  - ACOG, ESMO...
  - One report supports high intensity for low risk
    - Ueda et al. Int J Clin Oncol 2010; 15: 406 – 412

TABLE 2

## Endometrial cancer surveillance recommendations

Variable	Months			Years	
	0-12	12-24	24-36	3-5	>5
Review of symptoms and physical examination					
Low risk (stage IA grade 1 or 2)	Every 6 mo	Yearly	Yearly <sup>a</sup>	Yearly <sup>a</sup>	Yearly <sup>a</sup>
Intermediate risk (stage IB-II)	Every 3 mo	Every 6 mo	Every 6 mo <sup>b</sup>	Every 6 mo <sup>b</sup>	Yearly <sup>a</sup>
High risk (stage III/IV, serous or clear cell)	Every 3 mo	Every 3 mo	Every 6 mo	Every 6 mo	Yearly <sup>a</sup>
Papanicolaou test/cytologic evidence	Not indicated	Not indicated	Not indicated	Not indicated	Not indicated
Cancer antigen 125	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Radiographic imaging (chest x-ray, positron emission tomography/computed tomography, magnetic resonance imaging)	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use	Insufficient data to support routine use
Recurrence suspected	Computed tomography and/or positron emission tomography scan $\pm$ cancer antigen 125	Computed tomography and/or positron emission tomography scan $\pm$ cancer antigen 125	Computed tomography and/or positron emission tomography scan $\pm$ cancer antigen 125	Computed tomography and/or positron emission tomography scan $\pm$ cancer antigen 125	Computed tomography and/or positron emission tomography scan $\pm$ cancer antigen 125

<sup>a</sup> May be followed by a generalist or gynecologic oncologist; <sup>b</sup> Consider alternating visits with a generalist and gynecologic oncologist.

Salani. Surveillance for gynecologic cancers. *Am J Obstet Gynecol* 2011.

# Follow-up

- Who should conduct follow-up?
  - Multi-disciplinary

# Question

- Intensity/Interval?
- By whom?

# What we do not know

- Molecular Biology and all that weird stuff
- Management issues
  - HystBSO and LND
  - Adjuvant therapy
- Followup

