За матеріалами ISUOG 2014 IOTA (Internetional Ovarian Tumor Analysis) Яєчникові утворення

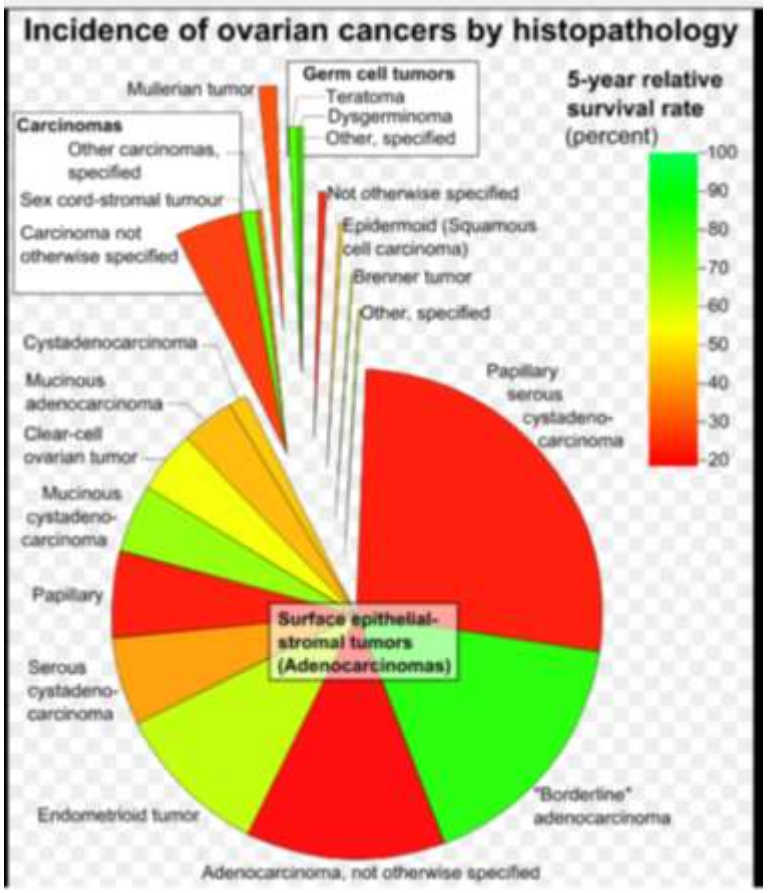
Судома Ірина

Рак яєчників

- В 2012 р рак яєчників було виявлено у 239,000 жінок
- Зафіксовано 152,000 смертей від раку ячників
- 3% від всіх раків у жінок, 8 місце за частотою смертей від раку у жінок

- Прогноз залежить від стадії хвороби
- 5 річна виживаємість у США при раку яєчників складає 45%

Percent of ovarian cancers in women age 20+	Histology	5 year RSR
89.7	Surface epithelial-stromal tumor (Adenocarcinoma)	54.4
26.4	Papillary serous cystadenocarcinoma	21.0
15.9	"Borderline" adenocarcinoma (underestimated b/c short data collection interval)	98.2
12.6	Adenocarcinoma, not otherwise specified	18.3
9.8	Endometrioid tumor	70.9
5.8	Serous cystadenocarcinoma	44.2
5.5	Papillary	21.0
4.2	Mucinous cystadenocarcinoma	77.7
4.0	Clear-cell ovarian tumor	61.5
3.4	Mucinous adenocarcinoma	49.1
1.3	Cystadenocarcinoma	50.7
5.5	Carcinoma	
4.1	Carcinoma not otherwise specified	26.8
1.1	Sex cord-stromal tumour	87.8
0.3	Other carcinomas, specified	37.3
1.7	Mullerian tumor	29.8
1.5	Germ cell tumor	91.0
0.8	Teratoma	89.1
0.5	Dysgerminoma	96.8
0.3	Other, specified	85.1
0.6	Not otherwise specified	23.0
0.5	Epidermoid (Squamous cell carcinoma)	51.3
0.2	Brenner tumor	67.9
0.2	Other, specified	71.7



Ovarian cancers are histologically and genetically divided into two types, Type I ar

Деякі факти

Ризик фактори

- Відсутність пологів (дітей) (гормональні?)
- Спадковість (генетичні- BRCA1, BRCA2)

Групи ризику

- Старші жінки, які не народжували
- Жінки, які мають родичів 1 і 2 ступеню з раком молочної залози, яєчників, прямої кишки, кишківника

Захисні чинники

- Пригнічення овуляції, яка ушкоджує епітелій яєчника і провокує запалення: пологи, протизаплідні пігулки, годування
- Перев'язка труб, видалення труб, видалення матки суттєво (dramatically☺) зменшують ризик виникнення рака яєчників

- ДРТ, можливо, приводять до збільшення пограничних пухлин яєчників
- Лікування неплідності, в тому числі і ДРТ, не спричиняють збільшення частоти раку яєчників
- СПКЯ та ендометріоз? – зв'язок не доведено

Діагностика пухлин яєчника

УЗД
Біохімічні маркери

Діагностика пухлин яєчника

- RMI -risk of malignancy index (RMI)
- RMI = ultrasound score x menopausal score x CA-125 level in U/ml

There are two methods to determine the ultrasound score and menopausal score, with the resultant RMI being called RMI 1 and RMI 2, respectively, depending on what method is used.[23]

Feature	RMI 1	RMI 2
Ultrasound abnormalities: • multilocular cyst • solid areas • bilateral lesions • ascites • intra-abdominal metastases	0 = no abnormality 1 = one abnormality 3 = two or more abnormalities	0 = none 1 = one abnormality 4 = two or more abnormalities
Menopausal score	1 = premenopausal 3 = postmenopausal	1 = premenopausal 4 = postmenopausal
CA-125	Quantity in U/ml	Quantity in U/ml

An RMI 2 of over 200 has been estimated to have a sensitivity of 74 to 80%, a specificity of 89 to 92% and a positive predictive value of around 80% of ovarian cancer.[23] RMI 2 is regarded as more sensitive than RMI 1.[23]

RMI>200

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Improving strategies for diagnosing ovarian cancer: a summary of the International Ovarian Tumor Analysis (IOTA) studies

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KEYWORDS: biomarkers; decision support techniques; logistic models; ovarian neoplasms; ultrasonography

ABSTRACT

BACKGROUND

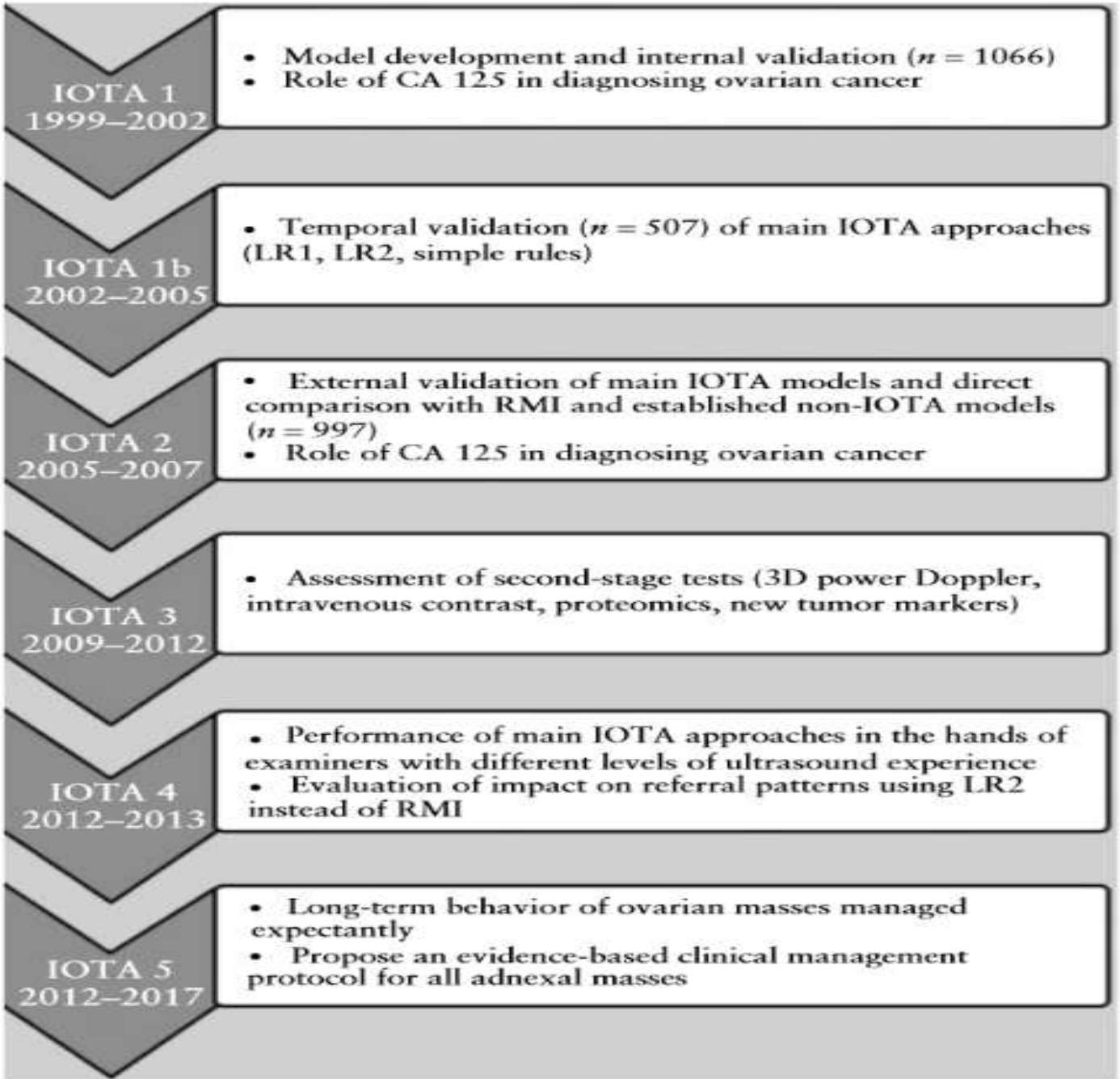
IOTA 1
1999–2002
• Model development and internal validation (n = 1066)
• Role of CA 125 in diagnosing ovarian cancer
IOTA 1b
2002–2005
• Temporal validation (n = 507) of main IOTA approaches (LR1, LR2, simple rules)
IOTA 2
2005–2007
• External validation of main IOTA models and direct comparison with RMI and established non-IOTA models (n = 997)
• Role of CA 125 in diagnosing ovarian cancer
IOTA 3
2009–2012
• Assessment of second-stage tests (3D power Doppler, intravenous contrast, proteomics, new tumor markers)
IOTA 4
2012–2013
• Performance of main IOTA approaches in the hands of examiners with different levels of ultrasound experience
• Evaluation of impact on referral patterns using LR2 instead of RMI
IOTA 5
2012–2017
• Long-term behavior of ovarian masses managed expectantly
• Propose an evidence-based clinical management protocol for all adnexal masses

Table 1 Diagnostic performance of the main predictive models and rules for discrimination between benign and malignant adnexal masses derived by the International Ovarian Tumor Analysis (IOTA) study and of the risk of malignancy index (RMI)

Model or rules	*IOTA phase*	*Type of validation*	n	*Sensitivity (%)*	*Specificity (%)*	*LR+*	*LR–*	*DOR*	*AUC*
LR1 (cut-off 10%)	1	Development data[26]	754	93	77	4.01	0.10	42.1	0.95
	1	Internal (test set)[26]	312	93	76	3.81	0.09	45.6	0.94
	1b	Temporal[27]	507	95	74	3.68	0.07	55.8	0.95
	2	Temporal[28,29]	941	93	81	4.77	0.09	52.8	0.94
	2	External[28,29]	997	92	87	6.84	0.09	75.7	0.96
LR2 (cut-off 10%)	1	Development data[26]	754	92	75	3.71	0.10	35.5	0.93
	1	Internal (test set)[26]	312	89	73	3.36	0.15	23.1	0.92
	1b	Temporal[27]	507	95	74	3.64	0.07	55.0	0.95
	2	Temporal[28,29]	941	89	80	4.42	0.14	32.7	0.92
	2	External[28,29]	997	92	86	6.36	0.10	66.1	0.95
Simple rules with	1	Development data[32]	1066	91	90	8.84	0.10	84.4	N/A
subjective expert	1b	Temporal[32]	507	92	90	9.08	0.09	106	N/A
assessment*	2	Temporal[37]	941	92	93	12.28	0.09	142	N/A
	2	External[37]	997	90	93	12.63	0.11	120	N/A
Subjective expert	1	N/A	1066	88	95	18.52	0.13	147	N/A
assessment	1b	N/A	507	90	93	12.63	0.11	120	N/A
	2	N/A	941	93	93	14.15	0.07	190	N/A
	2	N/A	997	87	92	11.00	0.14	80.7	N/A
RMI† (cut-off 200)	2	External[28]	997	67	95	12.7	0.34	36.8	0.91

*Results are shown for simple rules supplemented with subjective assessment of ultrasound findings when the rules did not apply. †Missing

Прості правила

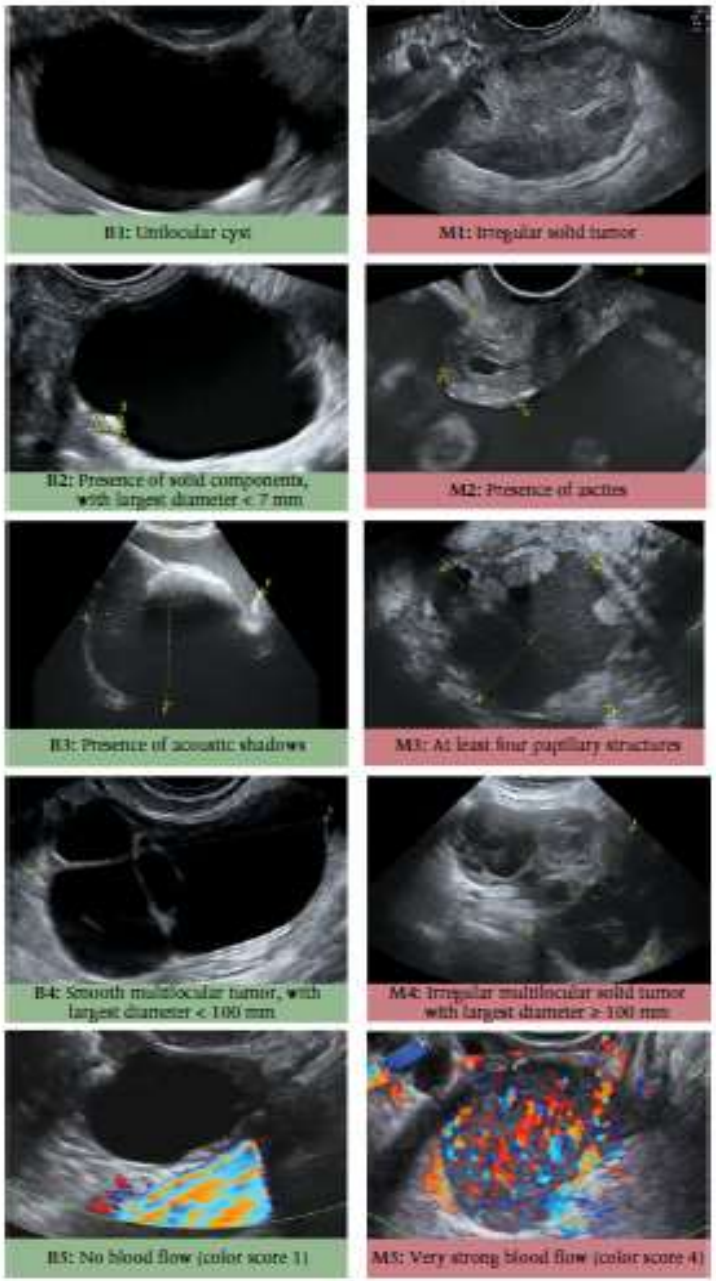

Figure 3 Ultrasound features used in the International Ovarian Tumor Analysis (IOTA) simple rules, illustrated by ultrasound images. B1–B5, benign features; M1–M5, malignant features.

Однокамерна кіста	**Неоднорідна щільна «солідна» пухлина**
Наявність щільного включення щонайбільше 7 мм	**Асцит**
Наявність акустичних тіней	**Щонайменше 4 папілярних включення**
Багатокамерна кіста з гладенькими перетинками	**Багатокамерна неоднорідна щільна пухлина**
Відсутність кровоплину (кольоровий індекс 1)	**Дуже сильний кровоплин (кольоровий індекс 4)**

Прості правила

- Доброякісні – якщо щонайменше 1 доброякісна риса і відсутні злоякісні
- Злоякісна – щонайменше 1 злоякісна і відсутні доброякісні
- Не визначені – вести, як потенційно злоякісні – експертна оцінка у спеціалізованому закладі
- 77% пухлин

Figure 5 International Ovarian Tumor Analysis (IOTA) 'easy descriptors' illustrated by ultrasound images. BD1–BD4, benign descriptors; MD1–MD2, malignant descriptors.

Легкі риси (easy descriptors)

Однокамерна кіста з мілкозернистим вмістом (ендометріома)	Однокамерна пухлина неоднорідної щільності і «тінню» (тератома)
Однокамерна кіста з гладенькими стінками щонайбільше 10 см (проста кіста або цистаденома)	Утворення з гладкими стінками сотоподібне, що залишається з попередніх Ме циклів (геморагічна кіста)
Пухлина з асцитом та, хоча б помірним кровоплином у постменопаузі	Вік після 50 років, Ca125 > 100 U/ml

Легкі риси

У випадках, де «легкі риси» могли бути застосовані

- Чутливість -98%, специфічність 97%
- Якщо є одна із легких рис – виставляється діагноз
- Якщо жодної риси немає, або є декілька – невизначена пухлина
- Застосовуються прості правила

Біомаркери

Ca 125

- Не покращує ефективність діагностики (вибору між доброякісністю і злоякісністю)
- Різниться між 2-4 стадіями раку яєчників та доброякісними пухлинами (окрім абсцесу та ендометріоми). Для всіх інших типів пухлин – значення суттєво накладаються.
- При порівнянні з УЗ за «простими правилами» IOTA і експертним УЗД – гірша діагностика
- Може з успіхом використовуватися для післяопераційного стеження за пацієнткою

He4 – Human epididymus secretory protein 4

- Moore RG et al.,Gynecol Oncol 2008 Комбінація двох маркерів суттєво покращує результати діагностики
- ROMA (risk of malignancy algorithm): комбінація Ca 125 і He4 та менопауза/неменопауза – специфічність 75%.
- Van Gorp et al. 2012 використовуючи IOTA правила та/або експертна УЗД – кращі результати ніж ROMA

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Ovarian cancer prediction in adnexal masses using ultrasound-based logistic regression models: a temporal and external validation study by the IOTA group

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Охарактеризувати яєчниковий утвір, як

1. **Доброякісний**
2. **Злоякісний**
3. **Пограничний**
4. **Первинно-інвазивний**
5. **Метастатичний**

Суб'єктивна оцінка експерта УЗ-діагноста

Безсумнівно доброякісна
Скоріше за все, доброякісна
Мабуть,доброякісна
Мабуть,злоякісна
Скоріше за все, злоякісна
Безсумнівно злоякісна

Subjective assessment
Certainly benign
Probably benign
Uncertain, benign
Uncertain, malignant
Probably malignant
Certainly malignant

Center	*Diagnosis* (n (%))				*Total* (n (%))
	Benign	*Primary invasive*	*Borderline*	*Metastatic invasive*	
External validation (new centers)	742 (74.4)	187 (18.8)	42 (4.2)	26 (2.6)	997 (100)
Genk, Belgium	173 (87)	21	5	1	200
Lublin, Poland	101 (66)	45	3	5	154
Cagliari, Italy	134 (87)	13	3	4	154
Bologna, Italy	124 (92)	6	3	2	135
Milan (B), Italy	41 (44)	36	10	7	94
Prague, Czech Republic	39 (43)	35	15	1	90
Beijing, China	57 (78)	12	1	3	73
Lund, Sweden	31 (82)	4	1	2	38
Milan (C), Italy	17 (81)	3	1	0	21
Udine, Italy	10 (59)	6	0	1	17
Ontario, Canada	11 (92)	1	0	0	12
Naples (B), Italy	4 (44)	5	0	0	9
Temporal validation (old centers)	654 (69.5)	186 (19.8)	69 (7.3)	32 (3.4)	941 (100)
Leuven, Belgium	155 (62)	60	24	13	252
Monza, Italy	199 (79)	31	17	4	251
Malmö, Sweden	110 (80)	21	6	0	137
Rome, Italy	54 (44)	49	11	8	122
London, UK	40 (62)	13	9	3	65
Naples (A), Italy	51 (80)	8	2	3	64
Milan (A), Italy	45 (90)	4	0	1	50
Total	1396 (72.0)	373 (19.2)	111 (5.7)	58 (3.0)	1938 (100)

Percentages are calculated per row.

Histological diagnosis	*All (n = 1938) (n (%))*	*Premenopausal (n = 1197)*	*Postmenopausal (n = 741)*	*Old centers (n = 941)*	*New centers (n = 997)*
Benign	1396 (72.0)	1014 (84.8)	382 (51.5)	654 (69.5)	742 (74.4)
Endometrioma	400 (20.6)	382 (31.9)	18 (2.4)	192 (20.4)	208 (20.9)
Serous cystadenoma	236 (12.2)	103 (8.6)	133 (17.9)	126 (13.4)	110 (11.0)
Teratoma	226 (11.7)	195 (16.3)	31 (4.2)	96 (10.2)	130 (13.0)
Mucinous cystadenoma	138 (7.1)	70 (5.9)	68 (9.2)	68 (7.2)	70 (7.0)
Simple cyst + parasalpingeal cyst	131 (6.8)	85 (7.1)	46 (6.2)	56 (6.0)	75 (7.5)
Fibroma	86 (4.4)	30 (2.5)	56 (7.5)	44 (4.7)	42 (4.2)
Functional cyst	77 (4.0)	68 (5.7)	9 (1.2)	27 (2.9)	50 (5.0)
Hydrosalpinx + salpingitis	49 (2.5)	47 (3.9)	2 (0.3)	22 (2.3)	27 (2.7)
Abscess	24 (1.2)	17 (1.4)	7 (0.9)	8 (0.9)	16 (1.6)
Rare benign	18 (0.9)	8 (0.7)	10 (1.3)	11 (1.2)	7 (0.7)
Peritoneal pseudocyst	11 (0.6)	9 (0.8)	2 (0.3)	4 (0.4)	7 (0.7)
Malignant	542 (28.0)	182 (15.2)	360 (48.5)	287 (30.5)	255 (25.6)
Primary invasive	373 (19.2)	101 (8.4)	272 (36.7)	186 (19.8)	187 (18.8)
Stage I	70 (3.6)	23 (1.9)	47 (6.3)	32 (3.4)	38 (3.8)
Stage II	30 (1.6)	7 (0.6)	23 (3.1)	12 (1.3)	18 (1.8)
Stage III	202 (10.4)	41 (3.4)	161 (21.7)	105 (11.2)	97 (9.7)
Stage IV	30 (1.6)	8 (0.7)	22 (3.0)	14 (1.5)	16 (1.6)
Rare primary invasive	41 (2.1)	22 (1.8)	19 (2.6)	23 (2.4)	18 (1.8)
Borderline	111 (5.7)	62 (5.2)	49 (6.6)	69 (7.3)	42 (4.2)
Stage I	99 (5.1)	52 (4.3)	47 (6.3)	63 (6.7)	36 (3.6)
Stage II	3 (0.2)	2 (0.2)	1 (0.1)	1 (0.1)	2 (0.2)
Stage III	8 (0.4)	7 (0.6)	1 (0.1)	4 (0.4)	4 (0.4)
Stage IV	1 (0.1)	1 (0.1)	0	1 (0.1)	0
Metastatic	58 (3.0)	19 (1.6)	39 (5.3)	32 (3.4)	26 (2.6)

Table 3 Demographic, clinical and ultrasound characteristics of the study population

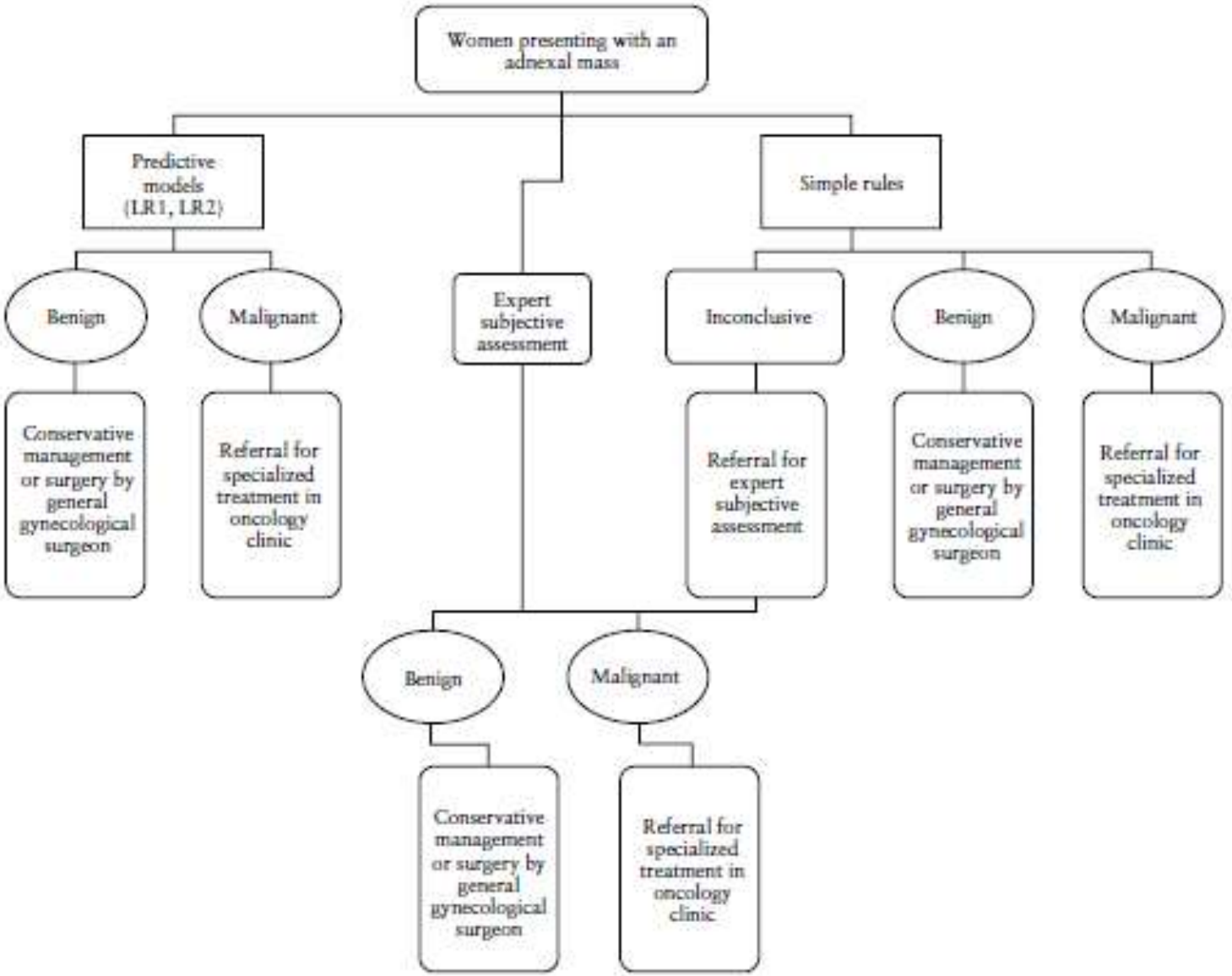
Variable	*External validation (new centers)*		*Temporal validation (old centers)*	
	Benign (n = 742)	*Malignant* (n = 255)	*Benign* (n = 654)	*Malignant* (n = 287)
Age (years, median)	40	56	41	57
Nulliparous	47.3	22.0	45.9	30.0
Personal history of ovarian cancer	0.4	3.5	1.2	4.5
Current use of hormonal therapy	12.0	6.3	13.5	7.3
Pain at ultrasound examination	24.1	11.0	14.5	11.5
Largest diameter of lesion (mm, median)	58	82	64	89
Solid component				
Present	27.2	94.9	29.8	89.9
Largest diameter (mm) if present (median)	24	51.5	26	54
Ascites	1.2	32.6	1.5	29.6
Papillations				
Present	10.0	31.4	11.8	38.0
Present, with blood flow	1.1	20.4	2.3	25.1
Irregular cyst walls	26.6	65.1	21.3	63.8
Acoustic shadows	19.1	5.9	15.3	4.2
Purely solid tumor	7.6	37.7	9.3	36.9
Subjective assessment				
Certainly benign	72.9	3.9	61.6	2.8
Probably benign	17.3	7.5	28.3	2.8
Uncertain, benign	1.9	1.2	3.5	1.4
Uncertain, malignant	3.0	2.8	2.9	8.0
Probably malignant	4.3	25.9	2.8	30.0
Certainly malignant	0.7	58.8	0.9	55.0

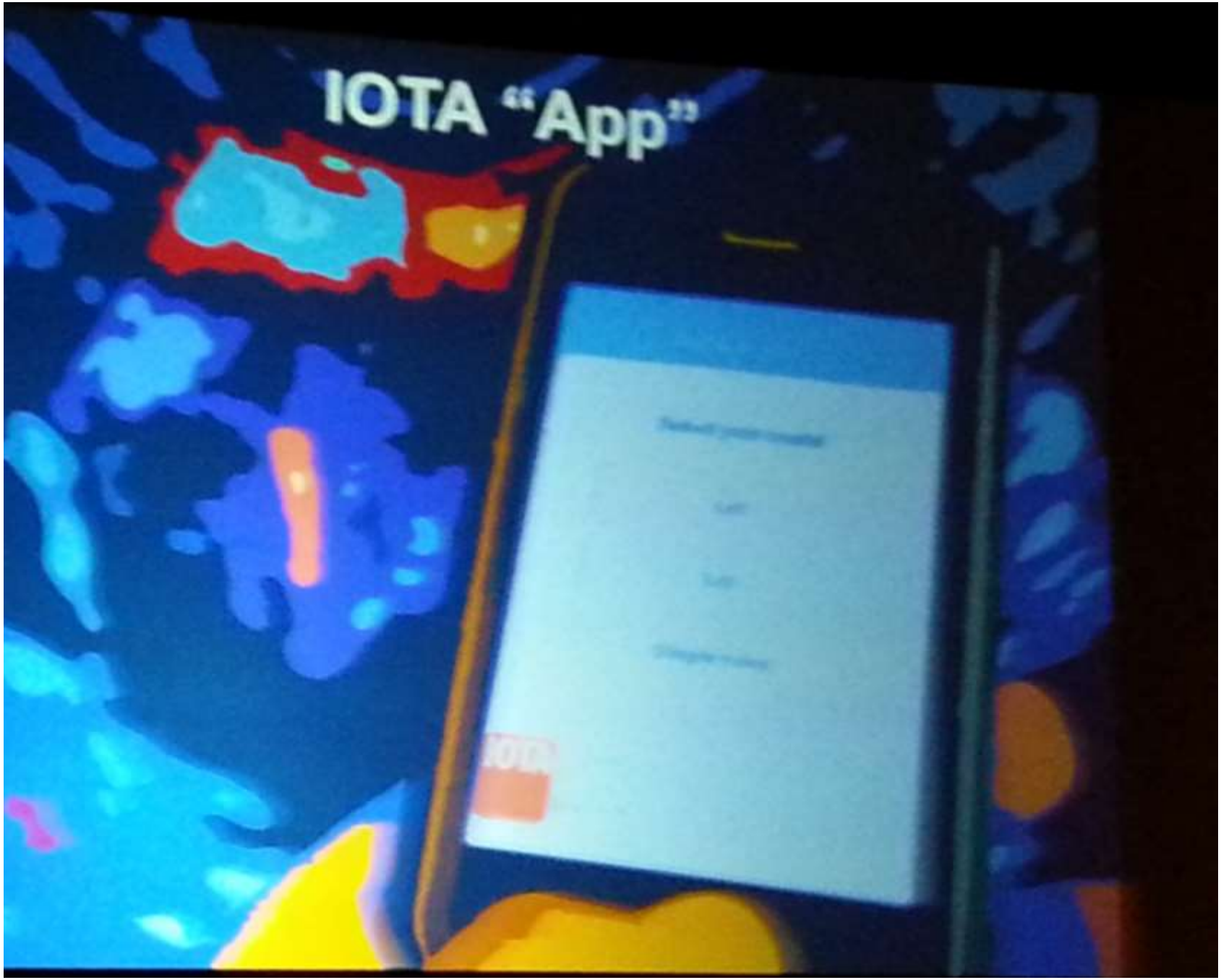
Data are expressed as % unless otherwise indicated.

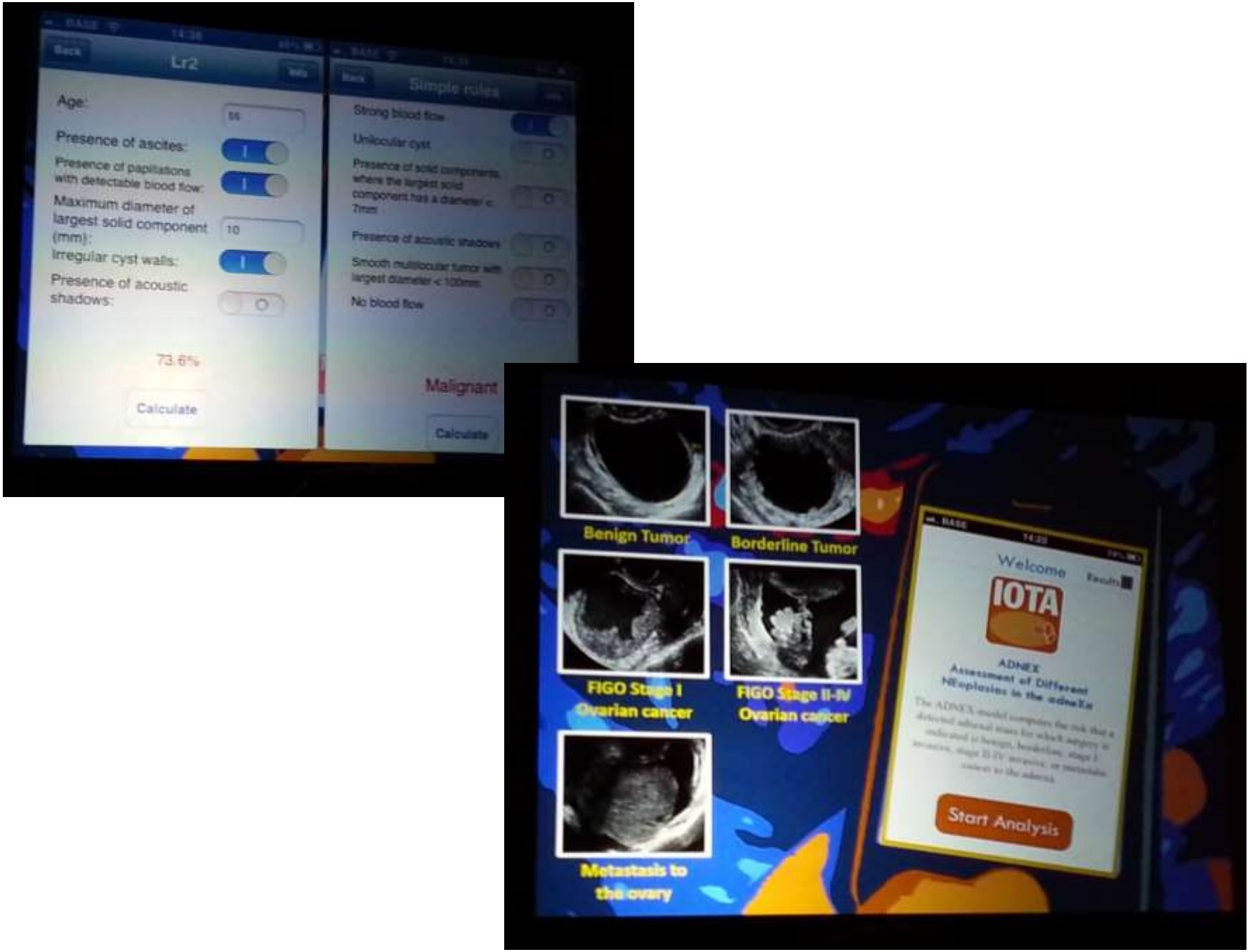
Висновки

On external validation we showed that the IOTA logistic regression models can predict the presence of ovarian malignancy in women with an adnexal mass and that the performance of the models is equivalent to subjective assessment by gynecologists and radiologists specialized in gynecological ultrasound examinations and who have a special interest in adnexal tumors. This is the first prospective study to externally validate the performance of IOTA logistic regression models to distinguish between benign and malignant adnexal masses. The simpler model containing six variables (LR2) performed almost as well as the model containing 12 variables (LR1). This is encouraging because a model with a small number of variables is likely to be more user-friendly.

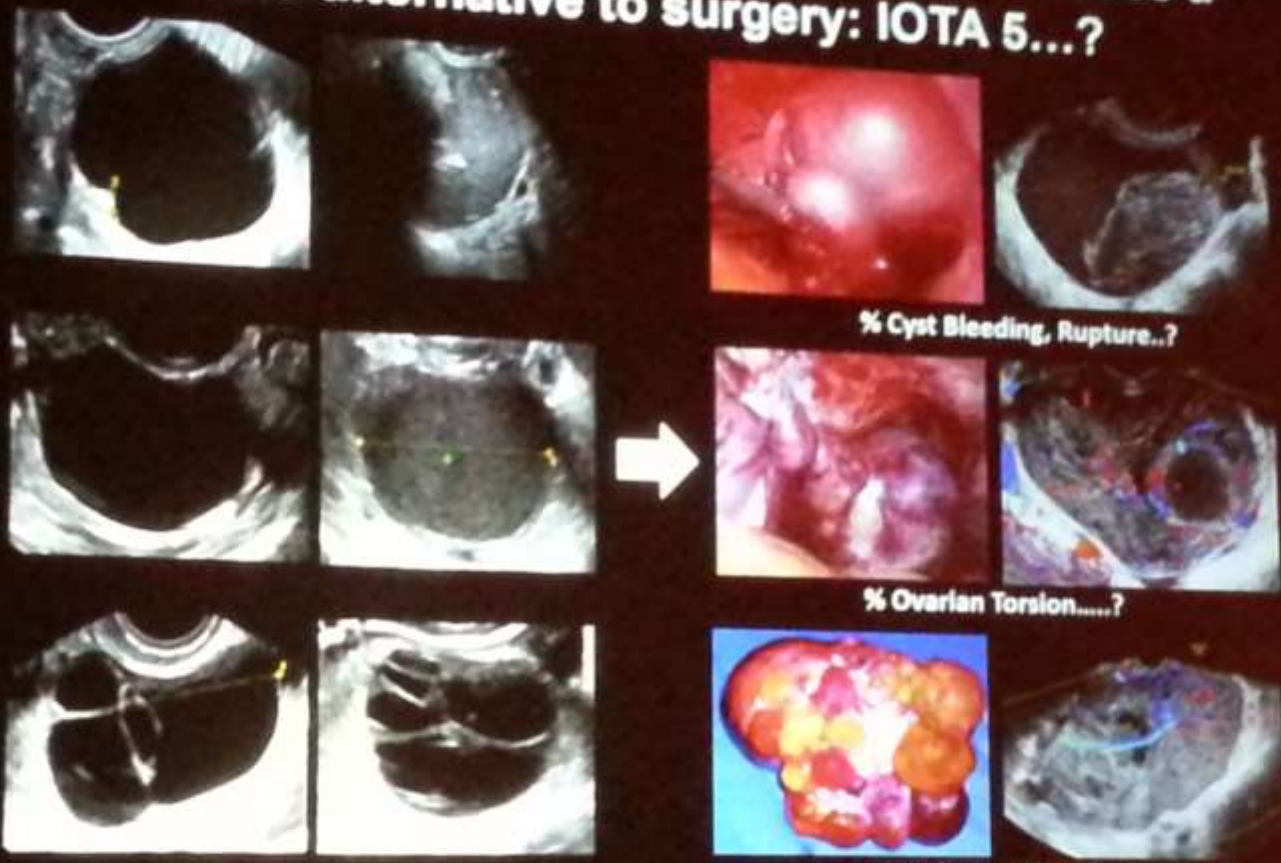
1. **LR1 та LR2 здатні прогнозувати наявність злоякісного утворення ТАК САМО, як спеціалісти**
2. **LR1 та LR2 майже однаково успішно прогнозують наявність злоякісного утворення**


Women presenting with an adnexal mass
Predictive models (LR1, LR2)
Simple rules
Benign
Malignant
Expert subjective assessment
Inconclusive
Benign
Malignant
Conservative management or surgery by general gynecological surgeon
Referral for specialized treatment in oncology clinic
Referral for expert subjective assessment
Conservative management or surgery by general gynecological surgeon
Referral for specialized treatment in oncology clinic
Benign
Malignant
Conservative management or surgery by general gynecological surgeon
Referral for specialized treatment in oncology clinic


IOTA "App"


Back
Lr2
Info
Age:
55
Presence of ascites:
Presence of papillations with detectable blood flow:
Maximum diameter of largest solid component (mm):
10
Irregular cyst walls:
Presence of acoustic shadows:
73.6%
Calculate
Back
Simple rules
Info
Strong blood flow
Unilocular cyst
Presence of solid components where the largest solid component has a diameter < 7mm
Presence of acoustic shadows
Smooth multilocular tumor with largest diameter < 100mm
No blood flow
Malignant
Calculate
Benign Tumor
Borderline Tumor
FIGO Stage I Ovarian cancer
FIGO Stage II-IV Ovarian cancer
Metastasis to the ovary
Welcome
IOTA
ADNEX
Assessment of Different NEoplasias in the adneXa
Start Analysis

Is expectant management for ovarian masses a safe alternative to surgery: IOTA 5…?



Граничні пухлини яєчників

- 15% всіх пухлин яєчника

Modern Pathology (2005) 18, S33–S50

www.modernpathology.org

Borderline epithelial tumors of the ovary

William R Hart[1,2]

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The concept and terminology of borderline epithelial tumors of the ovary have been controversial for over a century, in spite of the acceptance of a borderline category in almost all current classifications of ovarian tumors. Typically, borderline tumors are noninvasive neoplasms that have nuclear abnormalities and mitotic activity intermediate between benign and malignant tumors of similar cell type. Borderline tumors of all surface epithelial cell types have been studied. The most common and best understood are serous borderline tumors

1898 р Пфанненштіль описав папілярну цистаденому яєчника, клінічні характеристики якої були на межі між злоякісністю і доброякісноістю

The concept of borderline epithelial tumors of the ovary has faced controversy for over a century. In 1898, Hermann Johannes Pfannenstiel illustrated and described papillary ovarian cystadenomas with 'clinical features that stand on the border of malignancy'.[1] Similarly, Carl Abel in 1901 described proliferating papillary cystadenomas 'on the border line (sic) between benign and malignant growths'.[2] Howard Taylor introduced the term 'semi-malignant' tumor in 1929[3] and with his colleague Munnell delineated a 'borderline' category for a subset of serous cystadenocarcinomas in their historically important report on the clinical behavior of ovarian cancers.[4] The features of mucinous

Деякі факти

diate state of epithelial tumours of the ovary called 'borderline tumours'. Neither the oncological behaviour of this intermediate group of tumours nor the histological changes of the cells of the ovarian epithelium meet the specific criteria of benignity or malignancy. In 1973, the International Federation of Gynaecology and Obstetrics (FIGO) gave this group of ovarian tumours a 'low malignant potential' [1], and since then, the World Health Organization (WHO) has called them borderline ovarian tumours (BOTs) [2]

1973 р FIGO визначила ці пухлини, як пухлини «з низькою злоякісністю»
СОЗ (WHO) назвала їх граничними пухлинами яєчника (BOT - borderline ovarian tumours)

They are tumours that usually occur during the third to fourth decade of women's lives and are diagnosed as being limited to the ovary in 80% of cases. Because of this, their biological–oncological behaviour is very good, with an overall survival rate of ten years for 90% of those in the initial stages [3] and 60–70% of those in the advanced stages [4, 5].

У 80% випадків пухлина обмежена яєчниками
Виживання (5р) при ранніх стадіях – 90% (100%), при поширених пухлинах – 60-70% (90%)

Table 1. FIGO staging of borderline ovarian tumours.

Stage	
I	Tumour limited to the ovary
Ia	Tumour limited to an ovary, absence of malignant cells in ascites, intact capsule without tumour extension on the ovarian surface
Ib	Tumour limited to both ovaries, absence of malignant cells in ascites, intact capsule without tumour extension on the ovarian surface
Ic[a]	Presence of tumour cells in ascites or peritoneal lavage, presence of tumour on the ovarian surface of one or both ovaries, broken capsule
II	Condition of one or both ovaries with pelvic extension
IIa	Extension and/or in utero metastasis and/or fallopian tubes
IIb	Extension to other pelvic tissues
IIc[a]	IIa or IIb with the presence of tumour cells in ascites or peritoneal lavage, presence of tumour on the ovarian surface of one or both ovaries, broken capsule
III	The tumour compromises one or both ovaries with histologically confirmed peritoneal implants outside of the pelvis and/or positive pelvic lymph nodes. Superficial hepatic metastasis corresponds with stage III. The tumour is limited to the true pelvis but with histologically confirmed malignant extension in the small intestine or the omentum
IIIa	Tumour limited to the pelvis with negative nodes, positive peritoneal implants, or extension to the small intestine or the mesentery
IIIb	Condition of one or both ovaries with histologically confirmed implants, positive peritoneal metastasis, no more than 2 cm in diameter, and the nodes are negative
IIIc	Peritoneal metastasis beyond the pelvis > 2 cm in diameter and/or positive regional lymph nodes
IV	Condition of one or both ovaries with distant metastases. Positive pleural effusion. Metastasis of the hepatic parenchyma

[a] To assess the impact in the diagnosis of stages Ic or IIc, it would help to know if the rupture of the capsule was spontaneous or caused by the surgeon and if the source of the malignant cells detected was in the peritoneal lavage or ascites.

Within the next decade, a few large series of ovarian borderline or proliferative epithelial tumors were published.[8–11] The World Health Organization (WHO) applied the designation 'tumor of borderline malignancy' and added the synonym 'carcinoma of low malignant potential' (LMP) in their 1973 classification of ovarian tumors.[12] According to the WHO definition, a borderline epithelial tumor lacks obvious invasion of the stroma and has mitotic activity and nuclear abnormalities intermediate between clearly benign and unquestionably malignant tumors of a similar cell. Within the following

The absence of obvious stromal invasion is a principal diagnostic criterion for borderline tumors.

Відсутність явної інвазії в строму

Деякі факти

in the 20th century. For instance, a recent review of early-stage ovarian carcinomas from 1980 through 2000 at a leading cancer center resulted in reclassification of 29% of the cases as borderline tumors.[22] As a result, patients with Stage I borderline tumors often received adjuvant chemotherapy or radiation therapy, sometimes resulting in death due to therapy rather than the tumor.

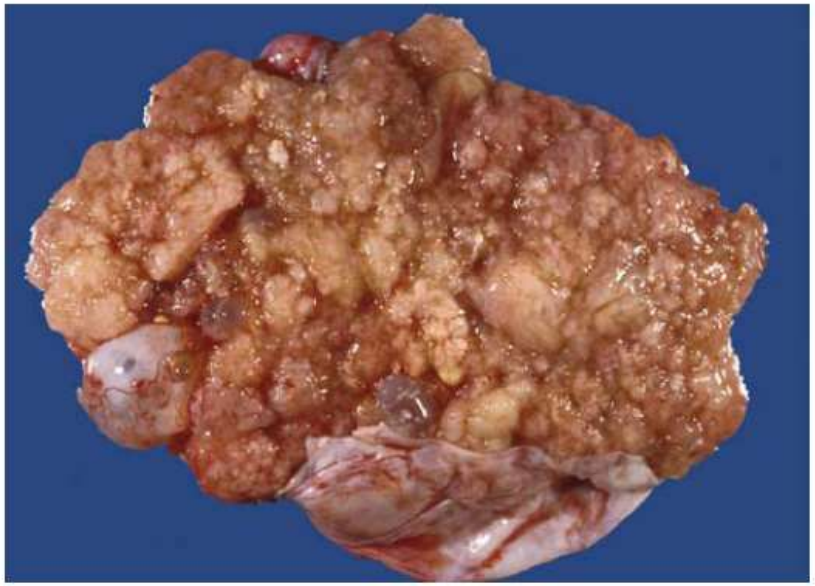


Figure 1 Papillary serous borderline tumor, entirely intracystic. Exuberant polypoid and papillary tumor protrudes from interior of cyst wall.

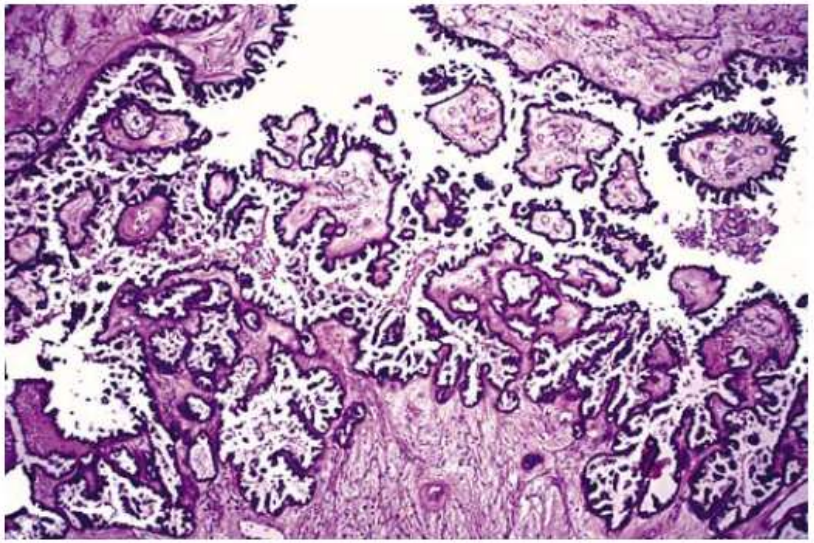


Figure 3 Papillary serous borderline tumor with hierarchical branching. Fibrous papillae are covered by proliferating epithelial cells with tufting and exfoliated cell clusters. Stromal invasion is absent.

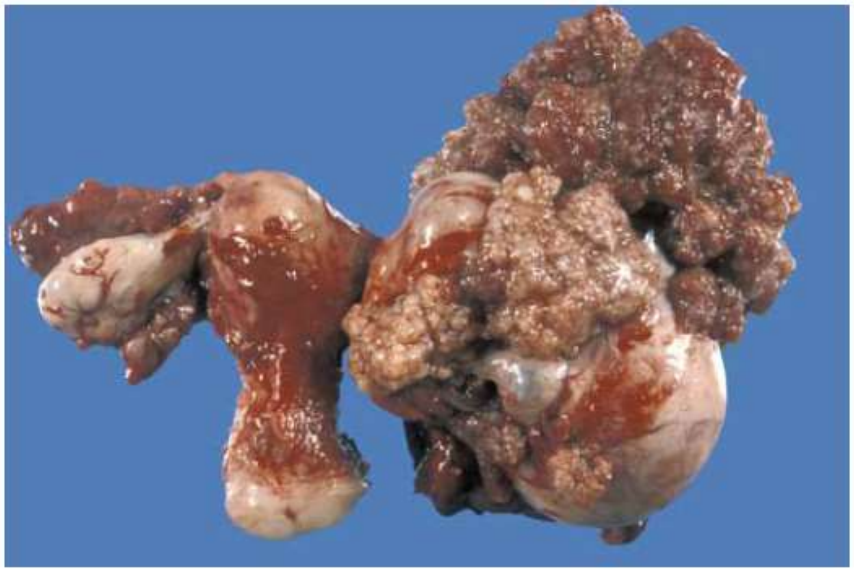


Figure 2 Papillary serous borderline tumor. Unilateral tumor with prominent surface exophytic component. Small serosal tumor implants are present on uterus and contralateral adnexa.

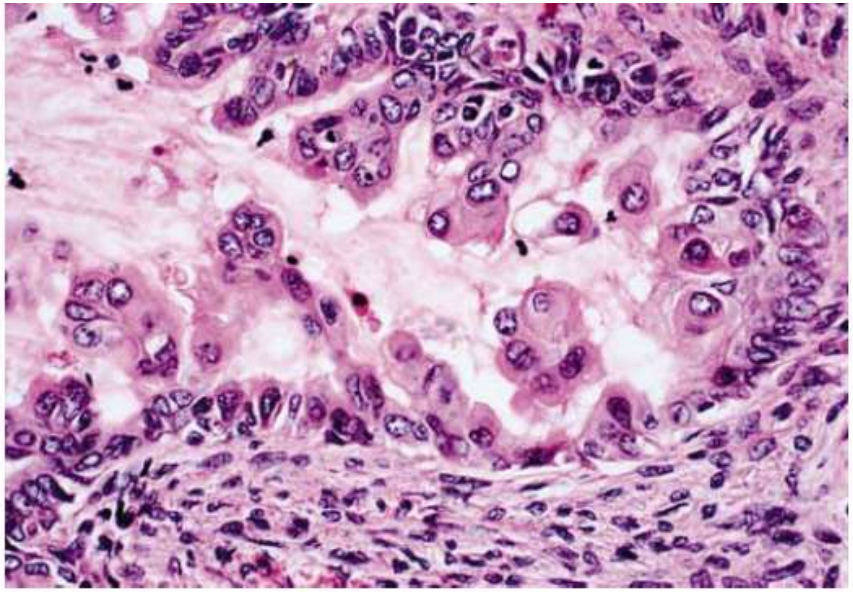


Figure 4 Papillary serous borderline tumor. Higher magnification of proliferating epithelial cells with low-grade nuclear atypia forming small tufts. Many of the cells have eosinophilic cytoplasm.

Мікроінвазія в строму

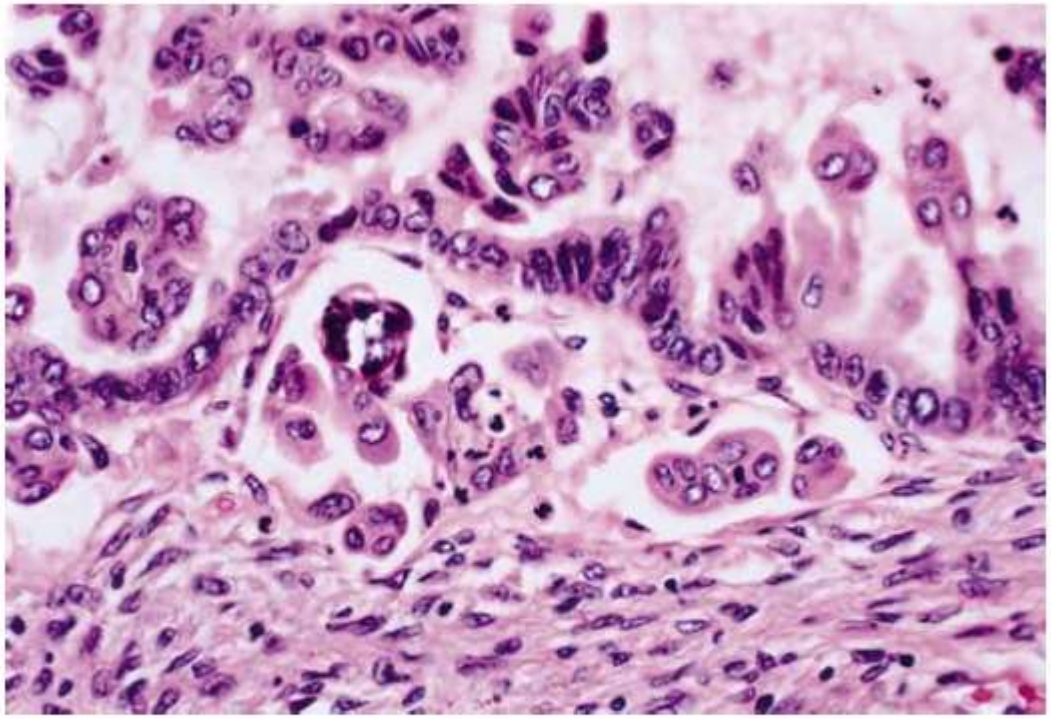


Figure 9 Serous borderline tumor with focal stromal microinvasion. Small clusters of eosinophilic epithelial cells with a psammoma body within nonvascular spaces are adjacent to a cyst lined by epithelial cells with similar cytologic features.

Імпланти неінвазивні

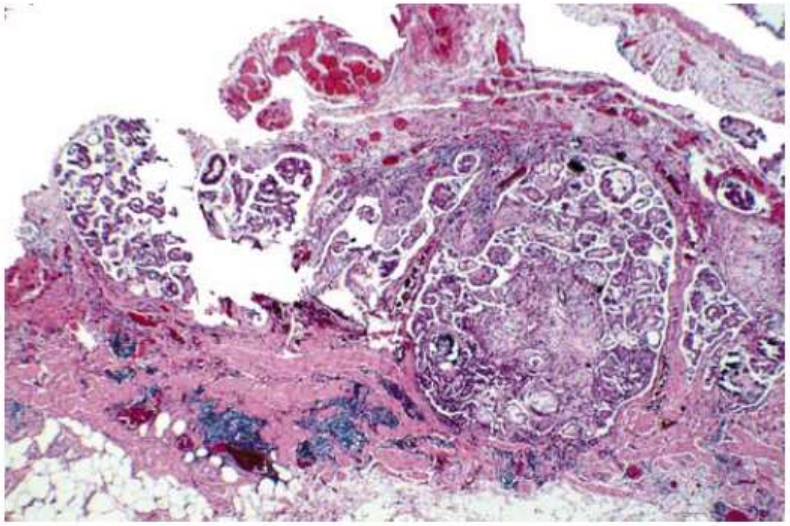


Figure 10 Peritoneal noninvasive epithelial implant of serous borderline tumor. The implant is plastered on the peritoneal surface. Focal desmoplasia is also present.

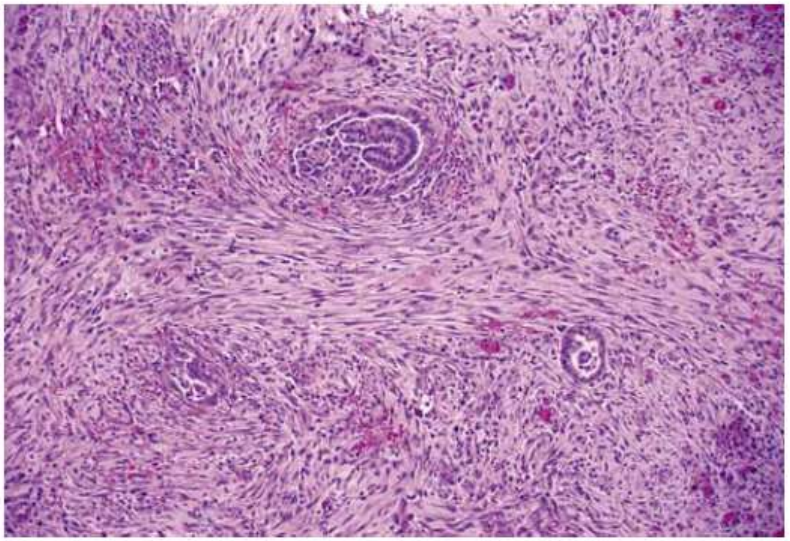


Figure 13 Higher magnification of desmoplastic noninvasive implant of serous borderline tumor seen in Figure 11. Small groups of tumor cells are embedded in inflamed connective tissue.

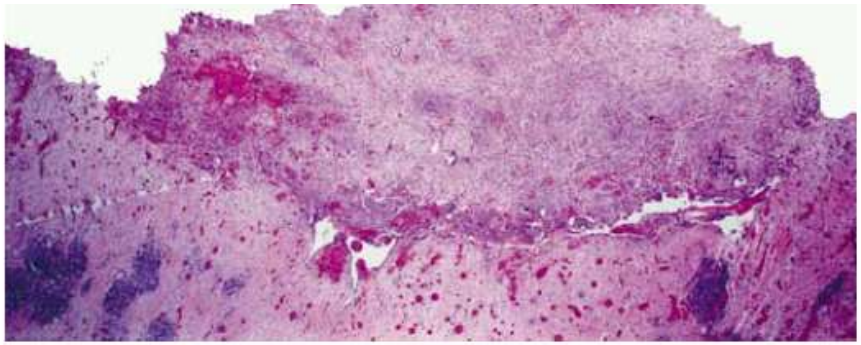


Figure 11 Noninvasive desmoplastic implant of serous borderline tumor is loosely adherent to the subjacent peritoneum. Most of the implant consists of cellular fibrous connective tissue. The neoplastic cells are not easily seen at this magnification.

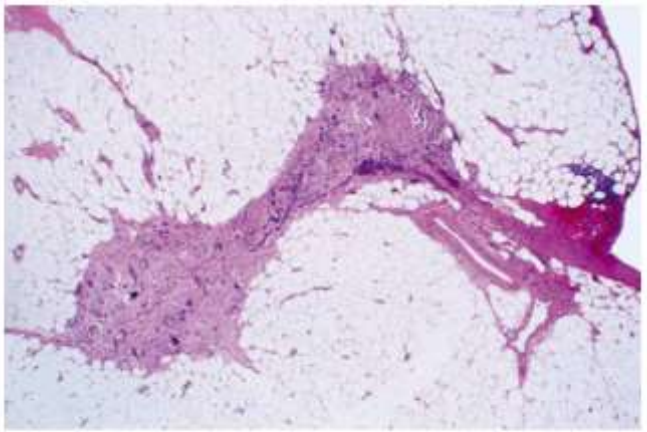


Figure 12 Omentum with a desmoplastic implant of serous borderline tumor extending between lobules of adherent adipose tissue, causing difficulty in determining whether the implant is invasive.

Імпланти інвазивні (14%)

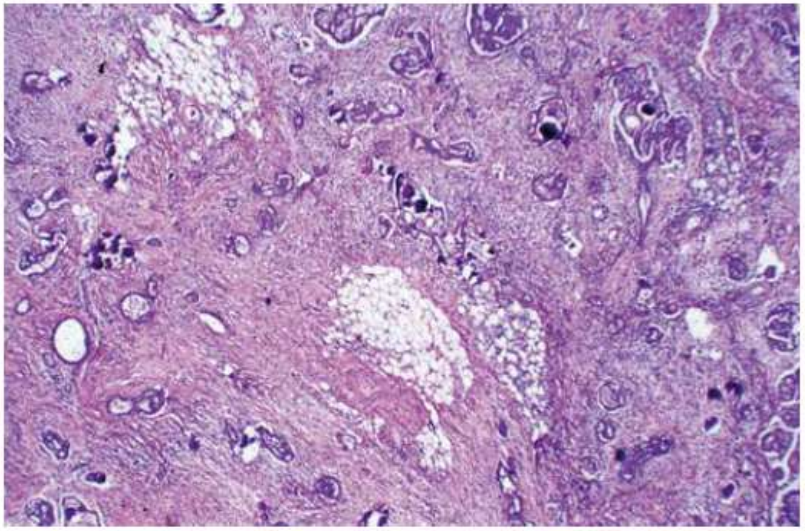


Figure 14 Omentum with a clearly invasive desmoplastic implant of serous borderline tumor. Only a small amount of residual adipose tissue remains.

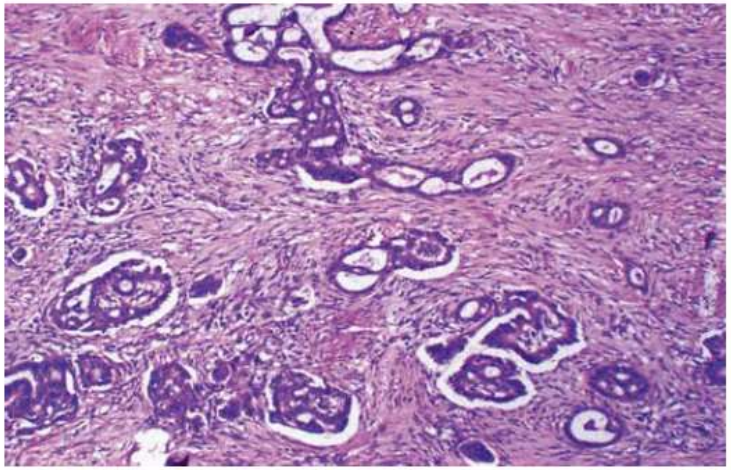
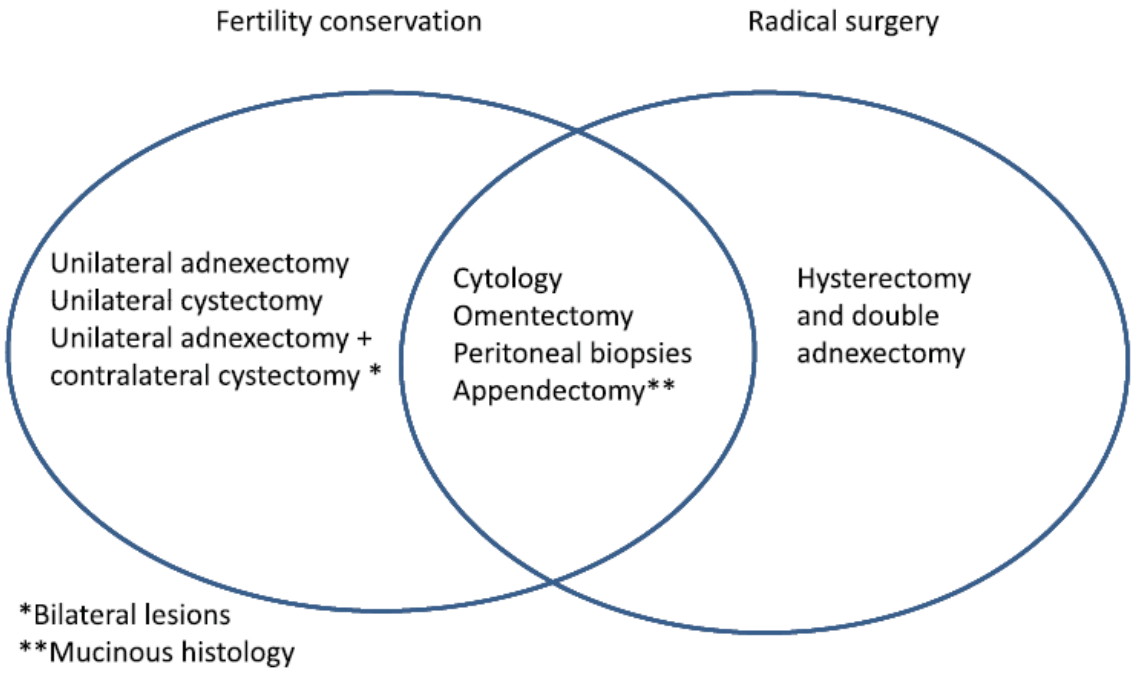


Figure 15 Higher magnification of omental invasive desmoplastic implant of serous borderline tumor. The neoplastic epithelial structures are more prominent and have complex architectural patterns with cribriform-like arrangements. Some are within clear spaces.

План дій за наявності ГПЯ



In contrast, the diagnosis may also be made at the time of the removal of a seemingly benign ovarian cyst. In that case, the dilemma is whether the patient should or should not be re-operated on, with the objective of completing the surgical staging and of making a careful inspection of the entire abdominal and pelvic cavity, to detect the presence of possible peritoneal implants. According to the data from the literature, this must be done mainly in the serous subtypes [33]. However, the majority of authors recommend this routinely, regardless of the histological subtype of the BOT [34, 35].

Збереження репродуктивної функції

Conservative fertility treatment

Conservative fertility treatment, which consists of removing the entire disease but preserving the uterus and at least a part of an ovary, is especially important in women with BOT since nearly 30% of women are diagnosed before 40 years old, and many of them have not even met their expectations for reproduction [8, 9]. The conservative treatment with BOT consists of doing peritoneal cytology, infracolic omentectomy, peritoneal biopsies, and appendectomy in the case of mucinous BOTs (Figure 1).

Conservative surgery has been extensively evaluated in recent years. After analysing more than 2000 published cases, conservative fertility surgery is associated with a major risk of recurrence of the disease but has no impact on the overall survival rate [48–50].

The radicalism of conservative surgery, either ovarian cystectomy or unilateral oophorectomy, must be based on the extension of the disease and the presence of factors associated with a bad prognostic advising against conservative treatment [11]. These include the presence of microinvasion, a micropapillary pattern, and invasive peritoneal implants [51]. In contrast, based on the data from the literature, there do not seem to be contraindications for the use of drugs for ovarian stimulation in case of getting future pregnancies following the diagnosis and treatment of the disease [52, 53].

Зберігаючі операції пов'язані із збільшенням ризику рецидивування хвороби
АЛЕ не впливають на рівень виживання пацієнтів

CASE REPORT

Ex-vivo oocyte retrieval for fertility preservation

Human M. Fatemi, M.D., Ph.D.,[a] Dimitra Kyrou, M.D.,[a] Majedah Al-Azemi, M.D.,[a] Dominique Stoop, M.D.,[a] Philippe De Sutter, M.D.,[b] Claire Bourgain, M.D., Ph.D.,[c] and Paul Devroey, M.D., Ph.D.[a]

[a] Department of Reproductive Medicine, [b] Department of Gynecology and Oncology, and [c] Department of Pathology, Academic Hospital at the Dutch-speaking Brussels Free University, Brussels, Belgium

Objective: To report a novel fertility preservation strategy in a woman with recurrent serous borderline ovarian tumor in the conserved ovary involving ex-vivo retrieval of in vivo matured oocytes and subsequent embryo cryopreservation.
Design: Case report.
Setting: Tertiary infertility care unit.
Patient(s): A 27-year-old woman presented for follow-up visit with a history of borderline serous adenocarcinoma treated conservatively with left oophorectomy and fertility-sparing laparoscopic staging. Ultrasound scan revealed a recurrent disease in the right ovary.
Intervention(s): Ex-vivo retrieval of mature oocytes after ovarian stimulation.
Main Outcome Measure(s): Fertility preservation.
Result(s): The patient underwent ovarian stimulation followed by a laparotomy and oophorectomy on the day of oocyte retrieval. A puncture of the follicles was performed in the operating theatre with a maximum ischemia time of 14 minutes. Eleven mature oocytes were aspirating, resulting in seven zygotes for cryopreservation.
Conclusion(s): Mature oocytes can be successfully retrieved ex-vivo from the oophorectomy specimen after a controlled ovarian hyperstimulation (COH) protocol. This method provides a possible strategy for fertility preservation in patients with recurrent ovarian cancer without the risk of cancer cells spillage associated with the standard transvaginal oocyte retrieval. (Fertil Steril® 2011;95:1787.e15–e17. ©2011 by American Society for Reproductive Medicine.)

Human Reproduction, Vol.24, No.4 pp. 850–855, 2009
Advanced Access publication on December 19, 2008 doi:10.1093/humrep/den459

human reproduction

ORIGINAL ARTICLE *Gynaecology*

Feasibility of ovarian cryopreservation in borderline ovarian tumours

V. Fain-Kahn[1], C. Poirot[2,3], C. Uzan[1], M. Prades[2], S. Gouy[1], C. Genestie[2], P. Duvillard[1], and P. Morice[1,4,5]

[1]Institut Gustave Roussy, Villejuif 94805, France [2]Groupe Hospitalier Pitié-Salpêtrière, Paris, France [3]UPMC Univ Paris 06, EA 1533, Paris F-75005, France [4]Univ Paris 11, Kremlin-Bicêtre, France

[5]Correspondence address. Institut Gustave Roussy, 39 rue Camille Desmoulins, Villejuif 94805, France. Tel: +33-1-42-11-51-34; Fax: +33-1-42-11-52-13; E-mail: morice@igr.fr

Human Reproduction, Vol.29, No.2 pp. 276–278, 2014
Advanced Access publication on December 9, 2013 doi:10.1093/humrep/det420

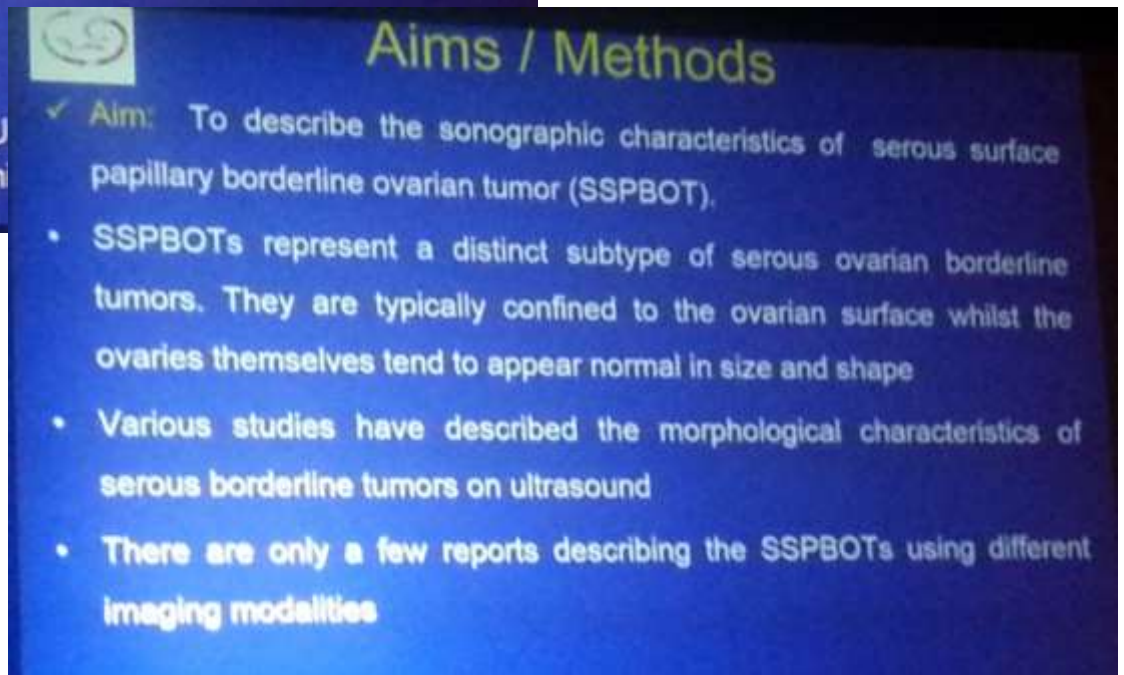
human reproduction

CASE REPORT *Infertility*

First pregnancy and live birth resulting from cryopreserved embryos obtained from *in vitro* matured oocytes after oophorectomy in an ovarian cancer patient

E.B. Prasath[1,4,*], M.L.H. Chan[1], W.H.W. Wong[1], C.J.W. Lim[1], M.D. Tharmalingam[1], M. Hendricks[1,4,5], S.F. Loh[1,2,4,5], and Y.N. Chia[3,6]

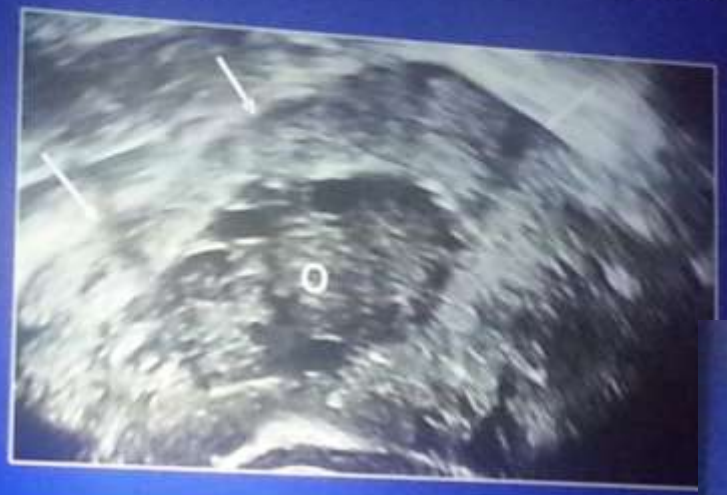

University College London Hospitals
NHS
24th World Congress on Ultrasound in Obstetrics and Gynecology
14–17 September 2014, Barcelona, Spain
OC 03.07 Ultrasound diagnosis of serous surface papillary borderline ovarian tumor: a case series
Manuela Ludovisi, Xulin Foo, Sara Mainenti, Antonia Carla Testa, Rupali Arora, Davor Jurkovic
Gynaecology Diagnostic and Treatment Unit, U
Dept of Obstetrics and Gynecology, Catholic Uni


Aims / Methods
Aim: To describe the sonographic characteristics of serous surface papillary borderline ovarian tumor (SSPBOT).
SSPBOTs represent a distinct subtype of serous ovarian borderline tumors. They are typically confined to the ovarian surface whilst the ovaries themselves tend to appear normal in size and shape
Various studies have described the morphological characteristics of serous borderline tumors on ultrasound
There are only a few reports describing the SSPBOTs using different imaging modalities

Case	Age	US findings RO	US findings LO	Ascites	US findings tumour deposit
1	29	Normal ovary surrondend by a 45mm* solid tumor	Normal	No	No
2	32	Mostly normal ovary with a 14mm* unilocular solid cyst and surrondend by solid tumor	Normal ovary surrondend by a 50mm* solid tumor	Yes	Yes
3	35	Mostly normal ovary with a 13mm* unilocular solid cyst and surrondend by solid tumor	Normal ovary surrondend by a 47mm* solid tumor	No	No
4	26	Normal ovary surrondend by a 45mm* solid tumor	50mm* multilocular solid lesion	Yes	Yes
5	36	57 mm* unilocular solid lesion	Normal ovary surrondend by a 51mm* solid tumor	No	No

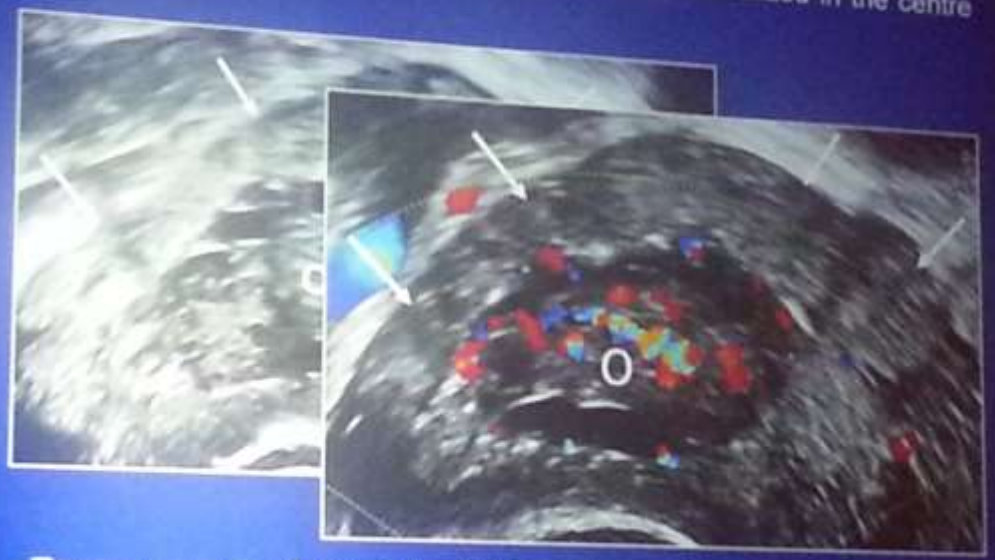
Results 1

In all cases transvaginal examination of the pelvis showed solid adnexal tumors with irregular surface and normal ovary visualized in the centre of the lesion.



Results 1

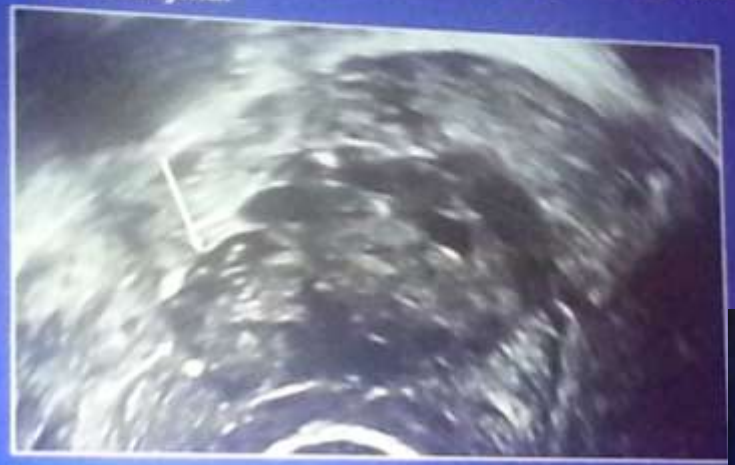
In all cases transvaginal examination of the pelvis showed solid adnexal tumors with irregular surface and normal ovary visualized in the centre of the lesion.



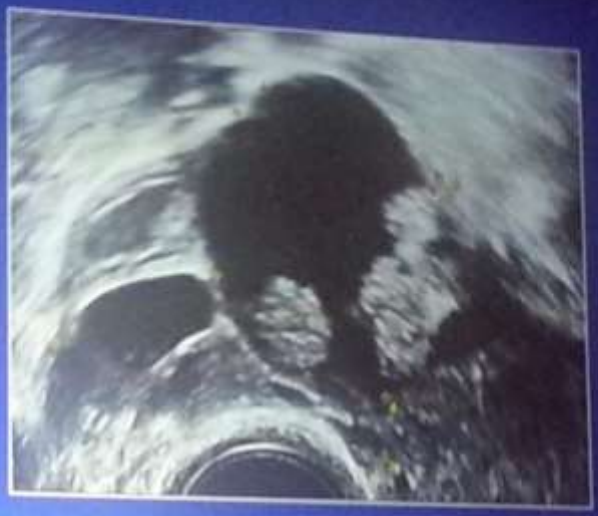
Tumors were poorly to moderately vascular on Doppler examination

Results 2

In two women (Cases 2 and 3) there were also very small unilocular/solid cysts within the right ovary surrounded by normal parenchyma.

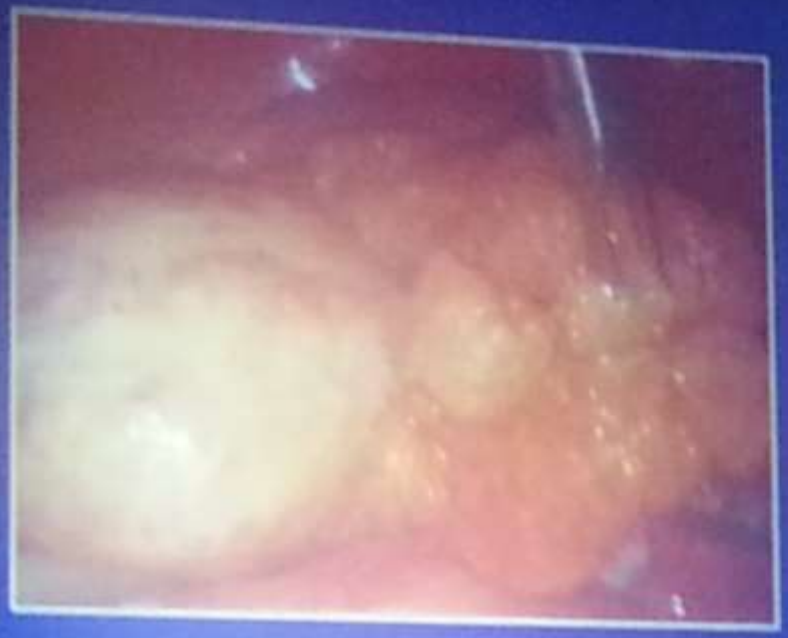


Results 2



Two women (Cases 4 and 5) had large cysts in contralateral ovaries which had typical appearances of serous borderline ovarian tumors. Normal ovarian parenchyma was seen adjacent to the cysts in both cases

Results 3



On histological examination two of our patients (Case 2 and 4) had a few **small microscopic foci suggestive of** low grade serous invasive cancer, but **these findings did not have a significant** impact on the management

Conclusion

- The appearances of the solid tumour component were non specific and the only finding which facilitated differential diagnosis form other malignant lesions was the presence of normal ovaries which were completely or partially surrounded by solid tumor tissue

- Identification of normal ovarian tissue adjacent to ovarian tumors ('ovarian crescent sign') has been shown to facilitate differential diagnosis between borderline ovarian tumor and invasive ovarian cancer.

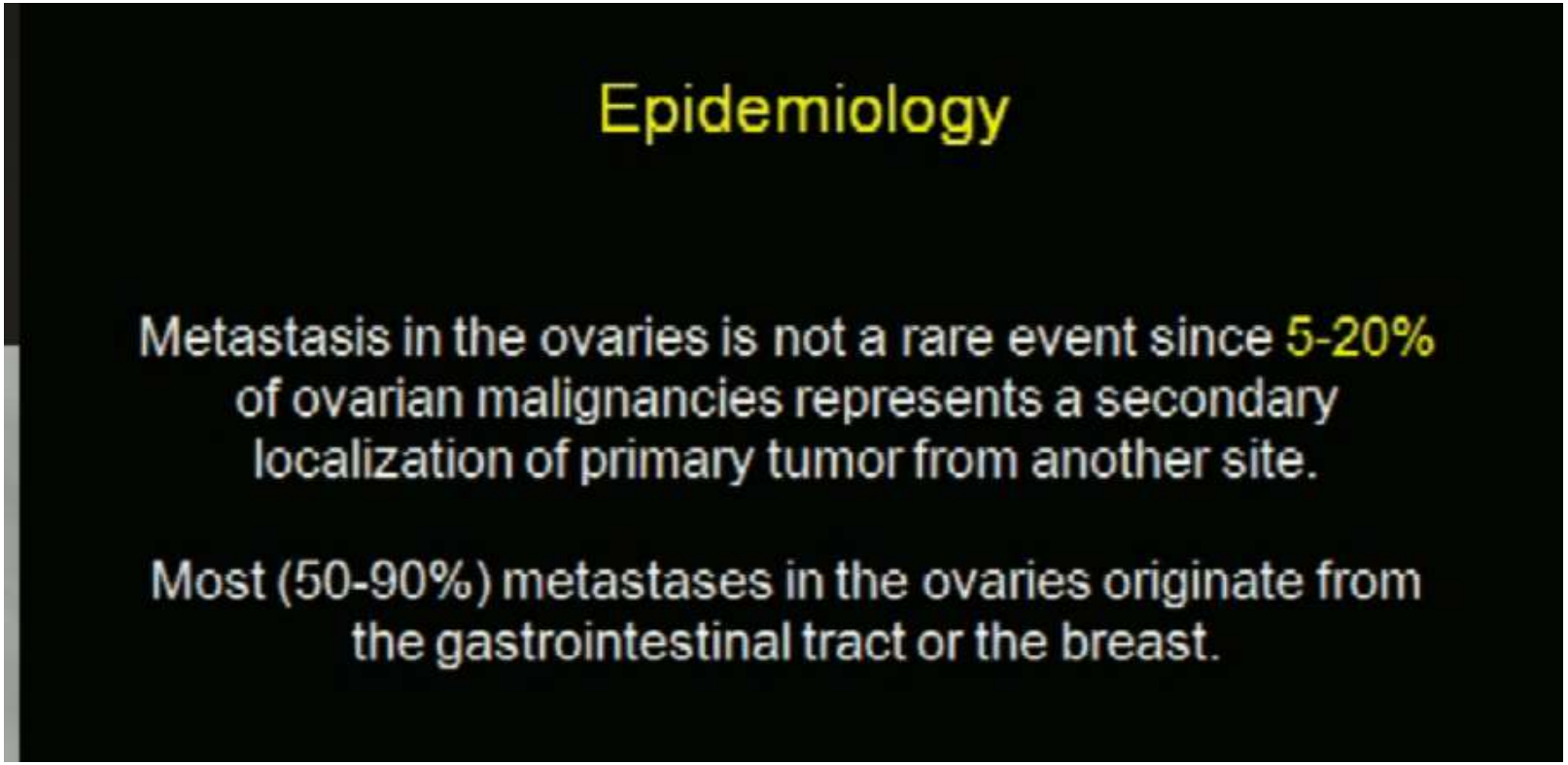
- Pre-operative detection of SSPBOT could have significant positive impact on the management of younger women in whom the preservation of reproductive capacity is of critical importance

- Further studies are needed to estimate the specificity of these ultrasound findings and the long term prognosis for women with SSPBOTs who underwent conservative, fertility-sparing surgery

Метастатичні пухлини

Ultrasound features of solid and "rare" subtypes of ovarian tumors

A. Testa, Italy

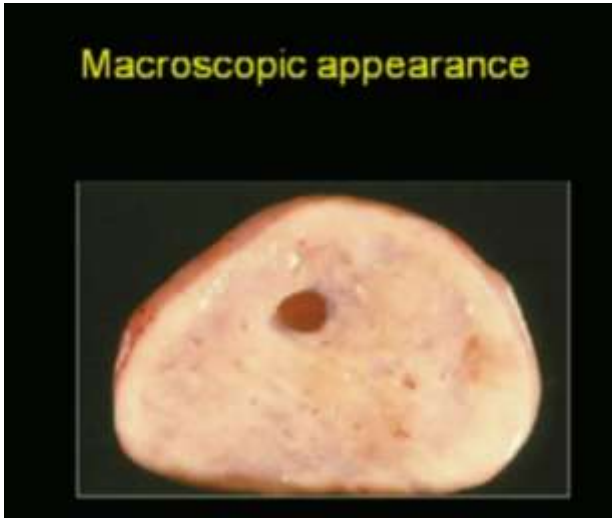


5-20% яєчникових злоякісних утворень є вторинними 50-90% походять з кишково-шлункового тракту та молочних залоз

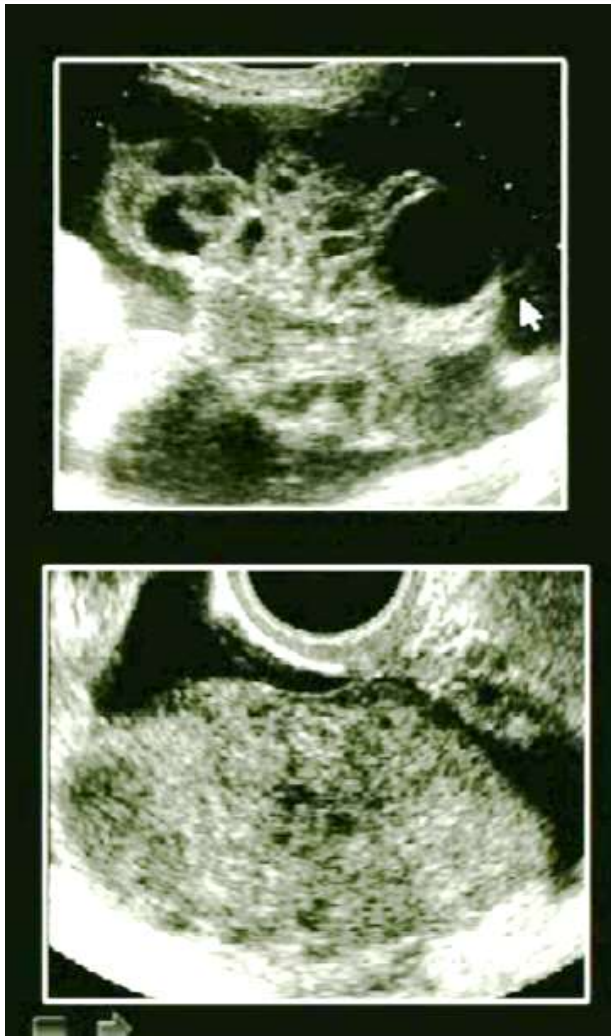
Типи пухлин

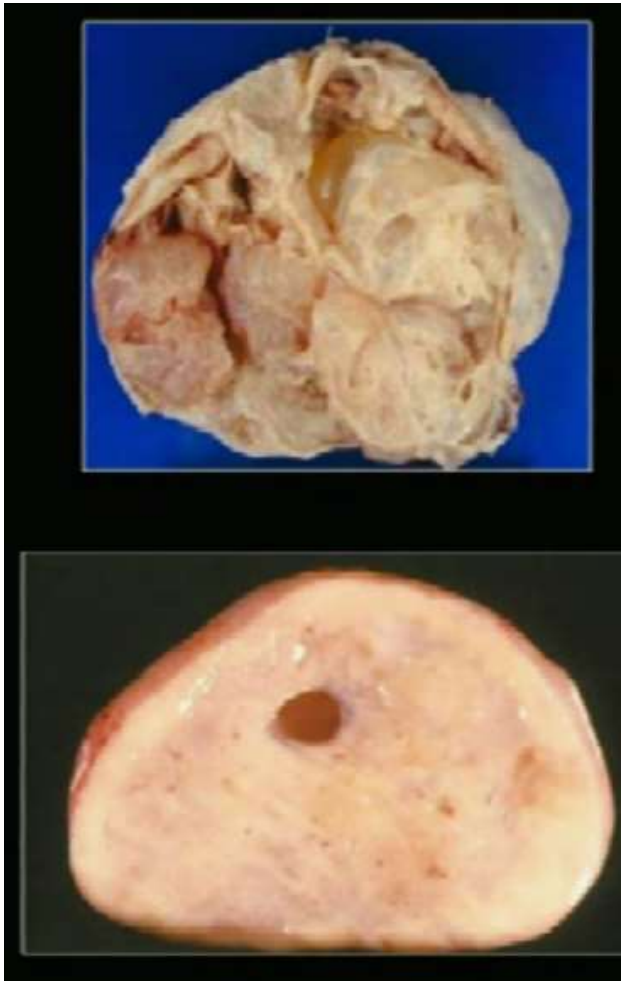
Багатокамерні щільні пухлини
Багатокамерні пухлини з щільним і кістозним компонентами
Пухлина Крукенберга

Двобічні пухлини

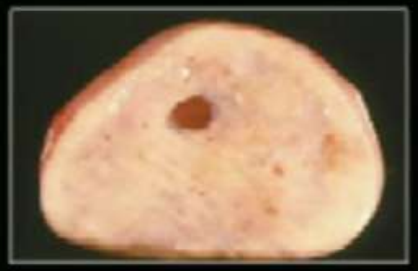


Найрозповсюдженіші типи метастатичних пухлин УЗ/вигляд пухлини





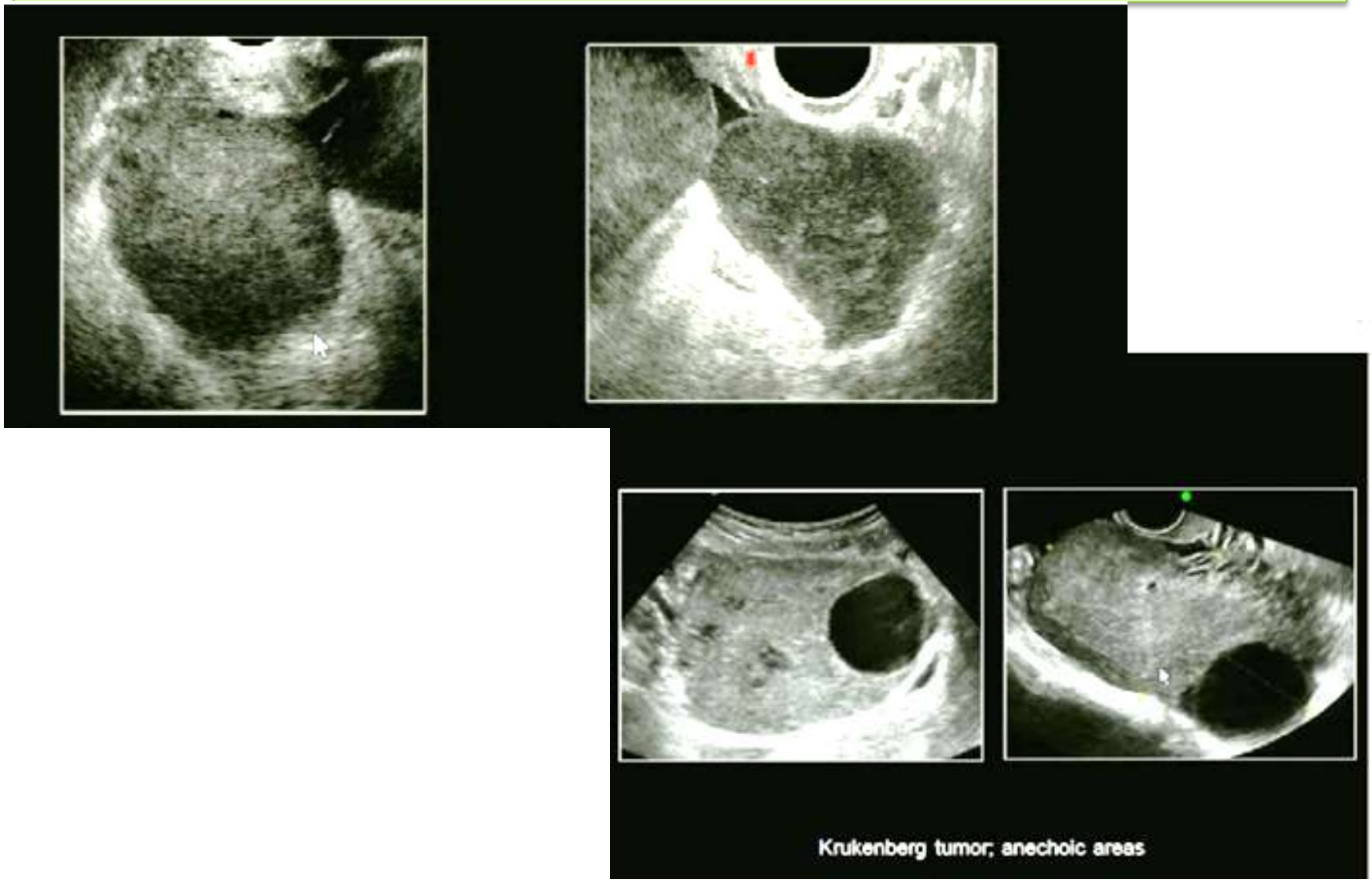
Microscopic appearance -2-



Krukenberg tumors are traditionally defined as composed of mucin-filled signet-ring cells associated with a striking proliferation of cellular non-neoplastic ovarian stroma.

The most common primary tumors in Krukenberg tumors are carcinoma of the stomach, large intestine, appendix and breast.

Пухлина Крукенберга



Ultrasound Obstet Gynecol 2007; 29: 505–511
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.4020

Imaging in gynecological disease (1): ultrasound features of metastases in the ovaries differ depending on the origin of the primary tumor

A. C. TESTA*, G. FERRANDINA*, D. TIMMERMAN†, L. SAVELLI‡, M. LUDOVISI*, C. VAN HOLSBEKE†, M. MALAGGESE*, G. SCAMBIA§ and L. VALENTIN‖

Results: symptoms and diagnosis

- In 29 (43%) of the 67 patients, the ovarian mass was detected at a planned follow-up visit because of previous diagnosis of a malignancy, and 17 (59%) of these patients were asymptomatic.

- In 38 (57%) patients, the pelvic mass was detected before the primary tumor was diagnosed, and 21 (55%) of these patients were symptomatic (bloating in 16 patients and pelvic pain in five patients).

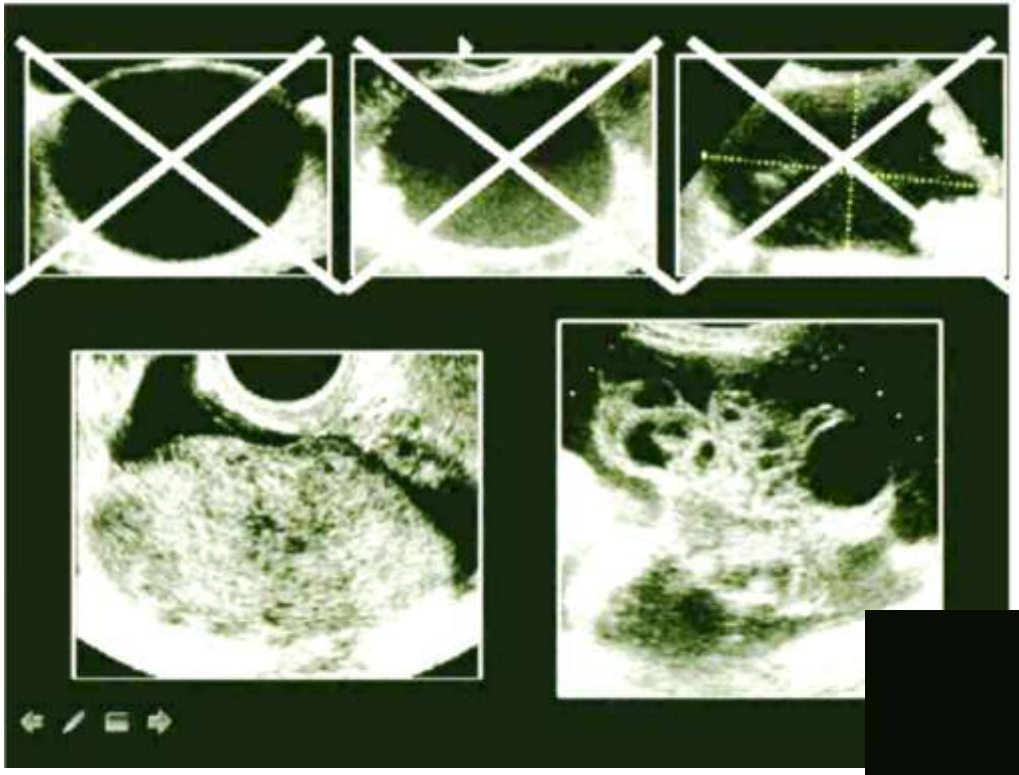
Results: CA 125

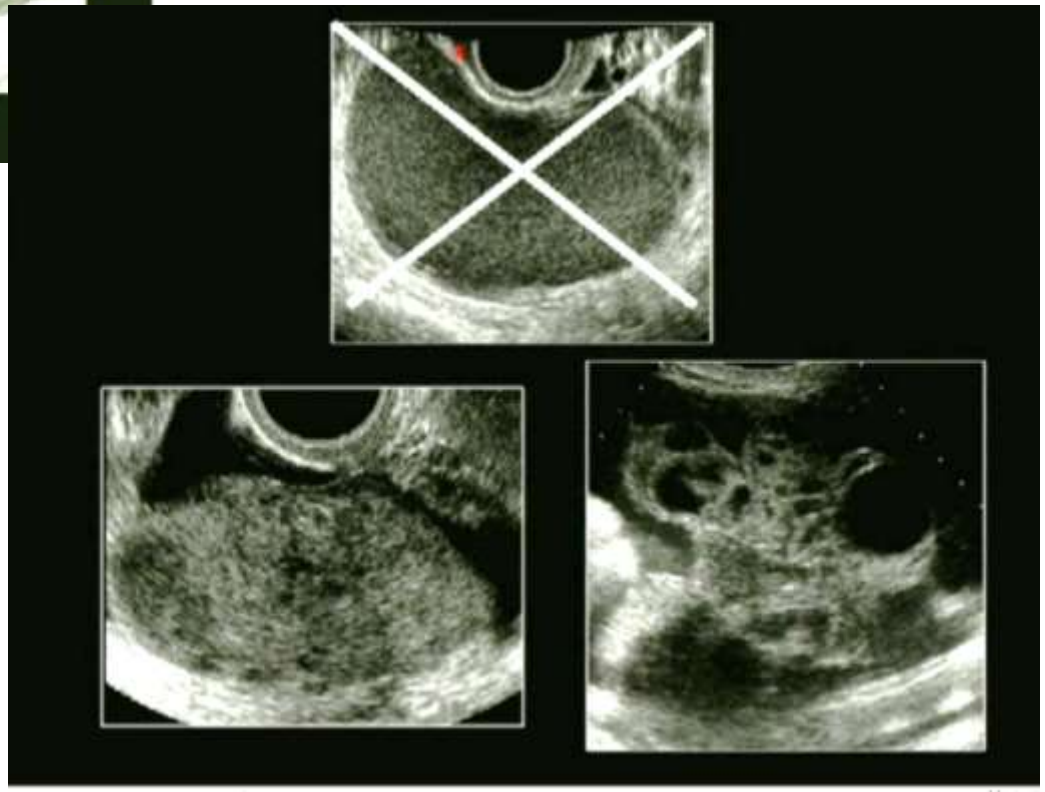
CA 125 was available in 43 patients, and 33 (77%) had a value greater than 35 U/mL (median 87, range 14 - 1648).

Results: ascites and bilaterality

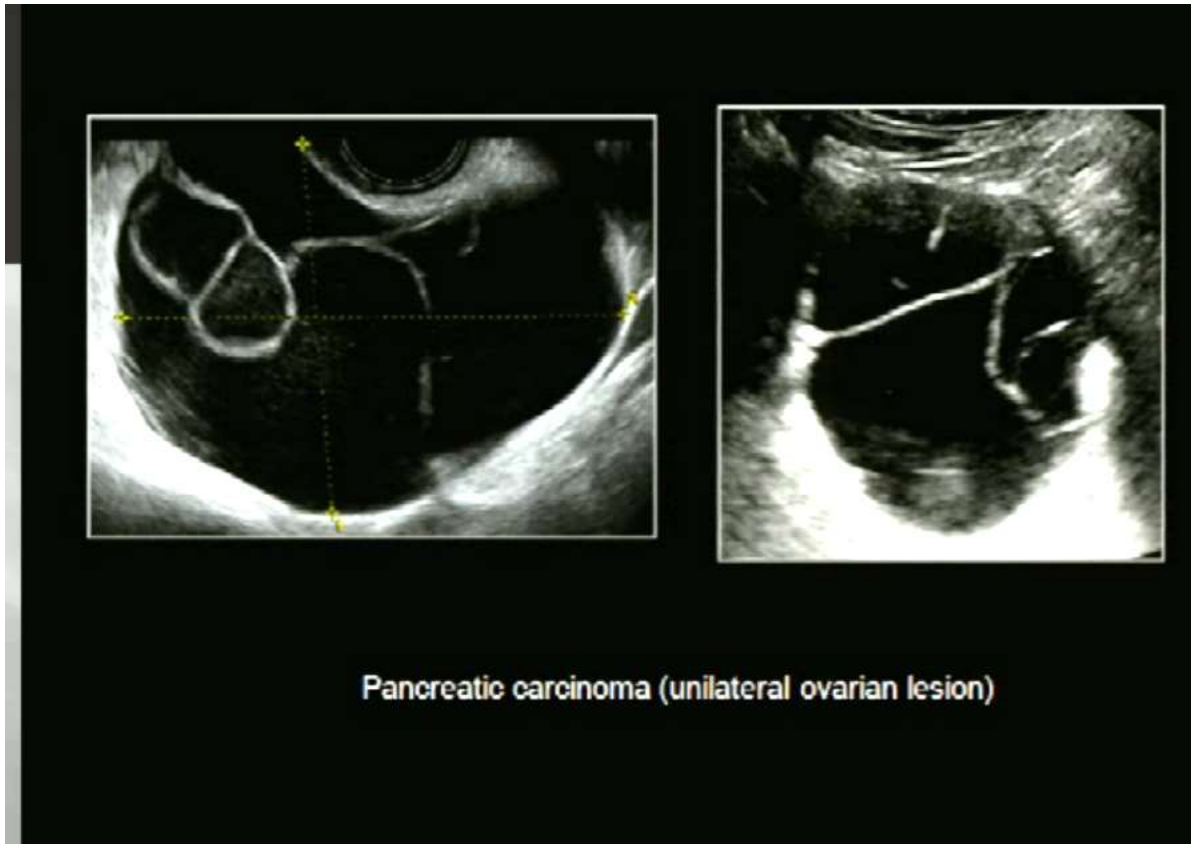
- The ovarian masses were associated with the presence of ascites in 39% of the cases.

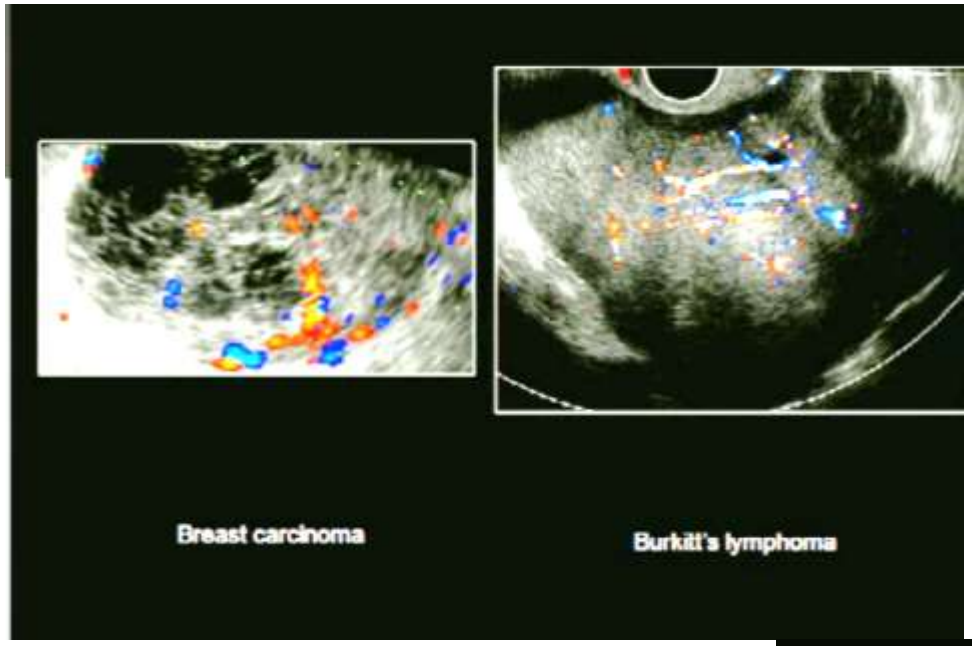
- At surgery 36 (54%) patients were found to have bilateral ovarian lesions.



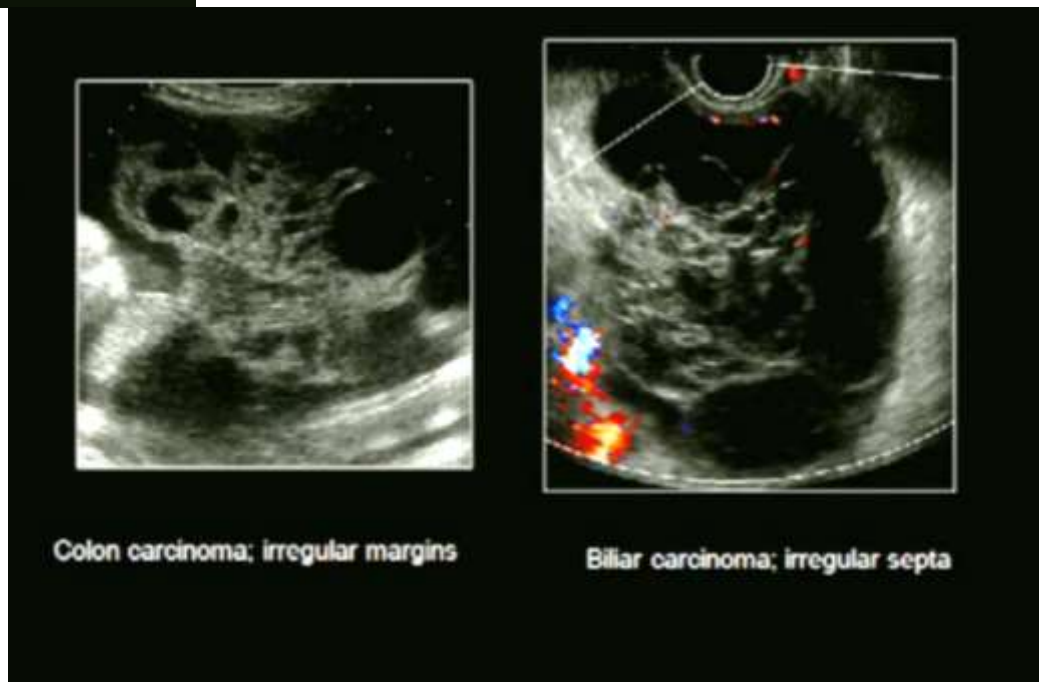


Не характерна структура



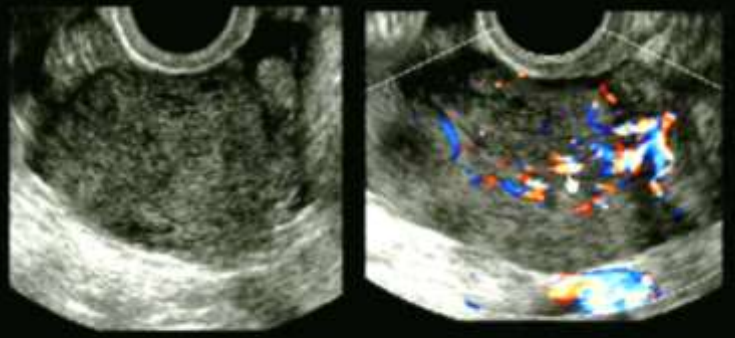


Не завжди все просто з кровоплином

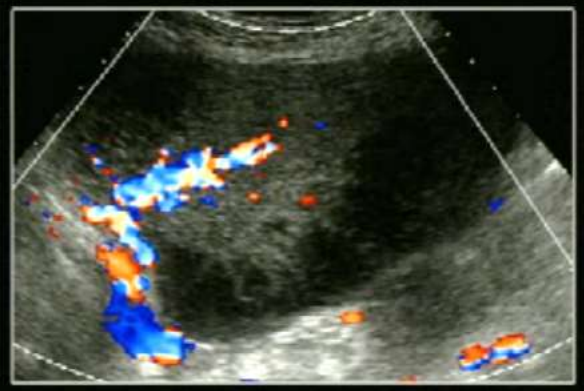


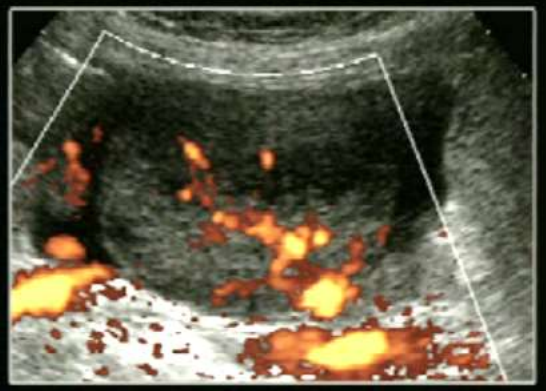
"Lead vessel"

... a main peripheral vessel which penetrates into the central part of the ovarian mass in a tree-shaped morphology.

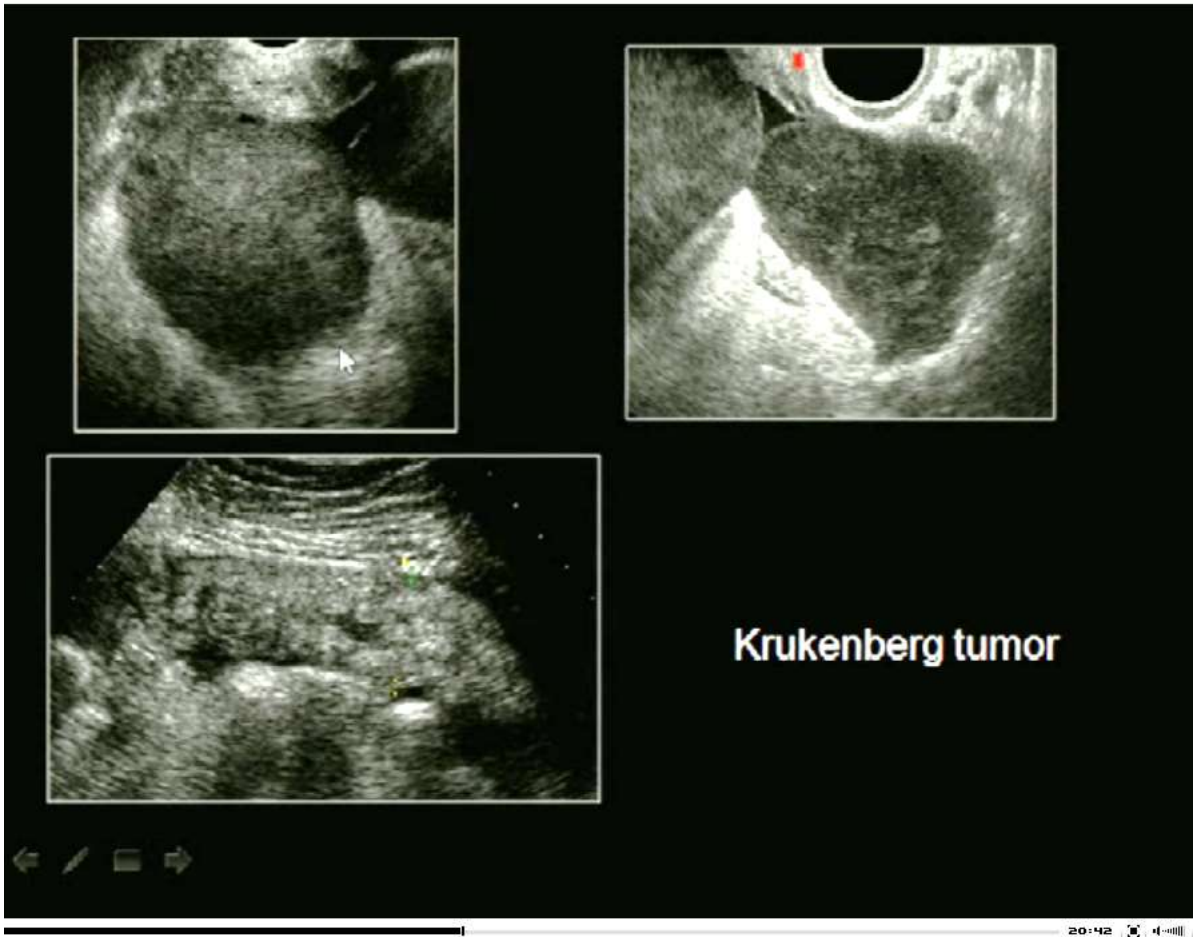


Lead vessel



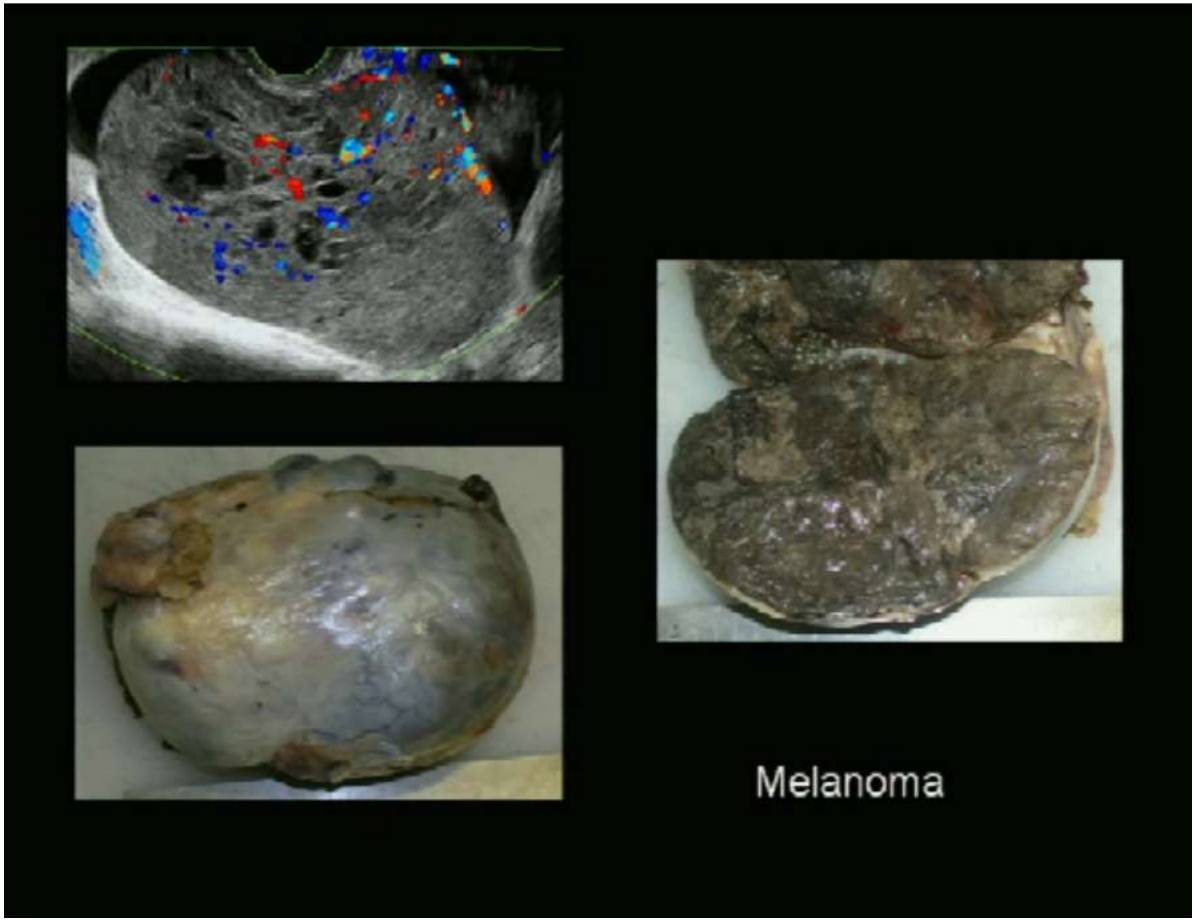


Пухлина Крукенберга. Сальник.

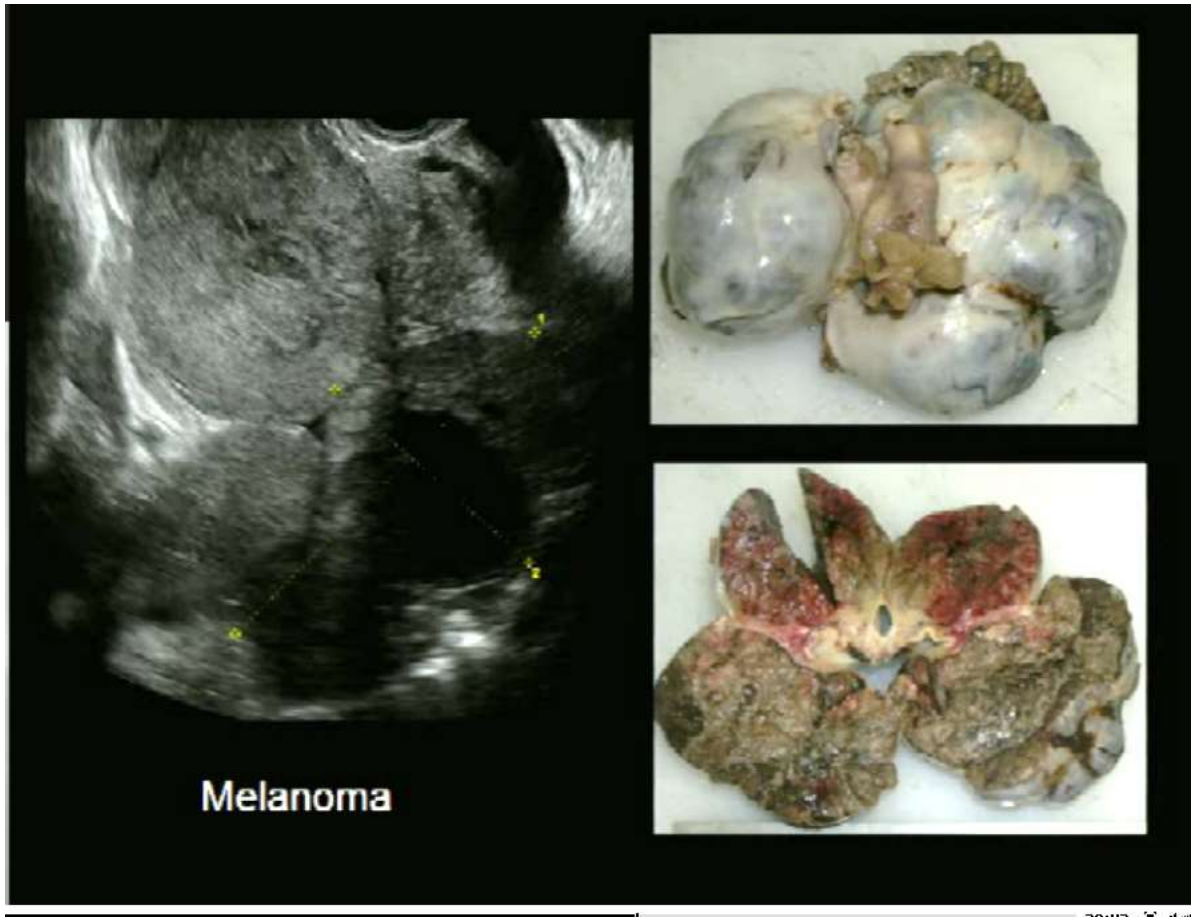


Рідкісні випадки

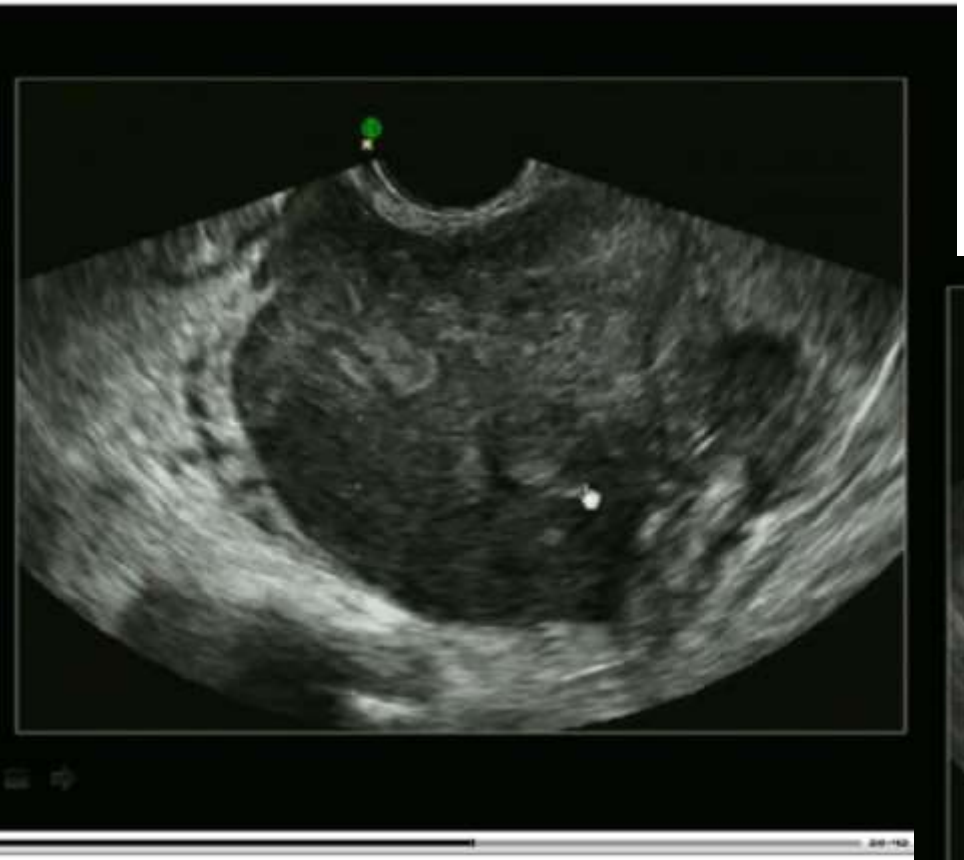
№1

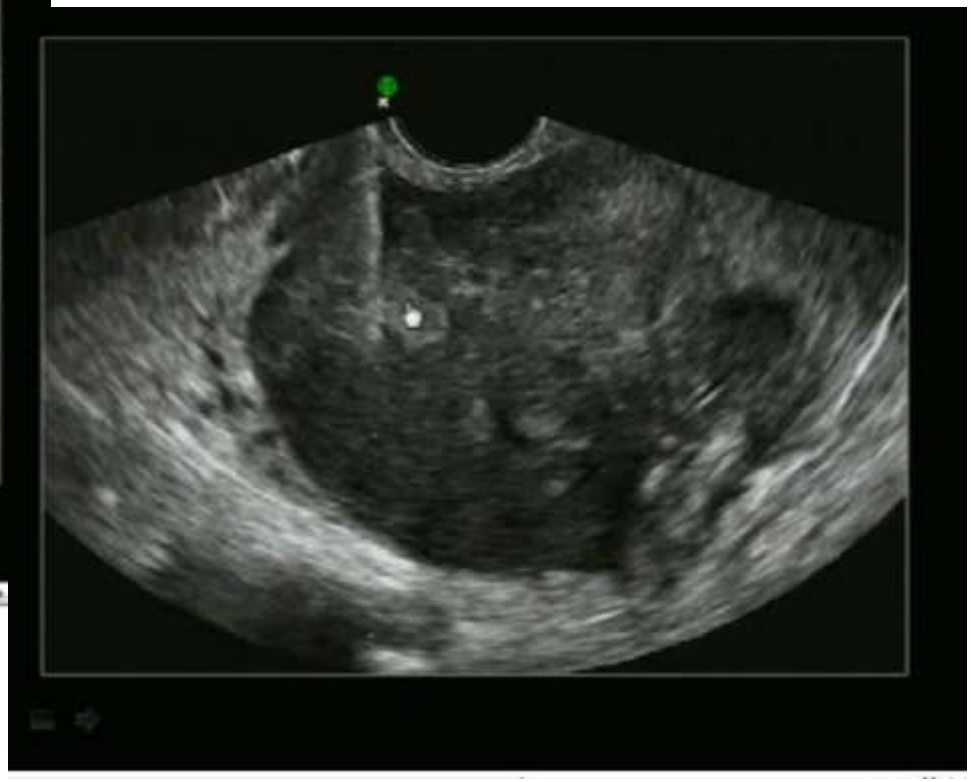


Інший яєчник



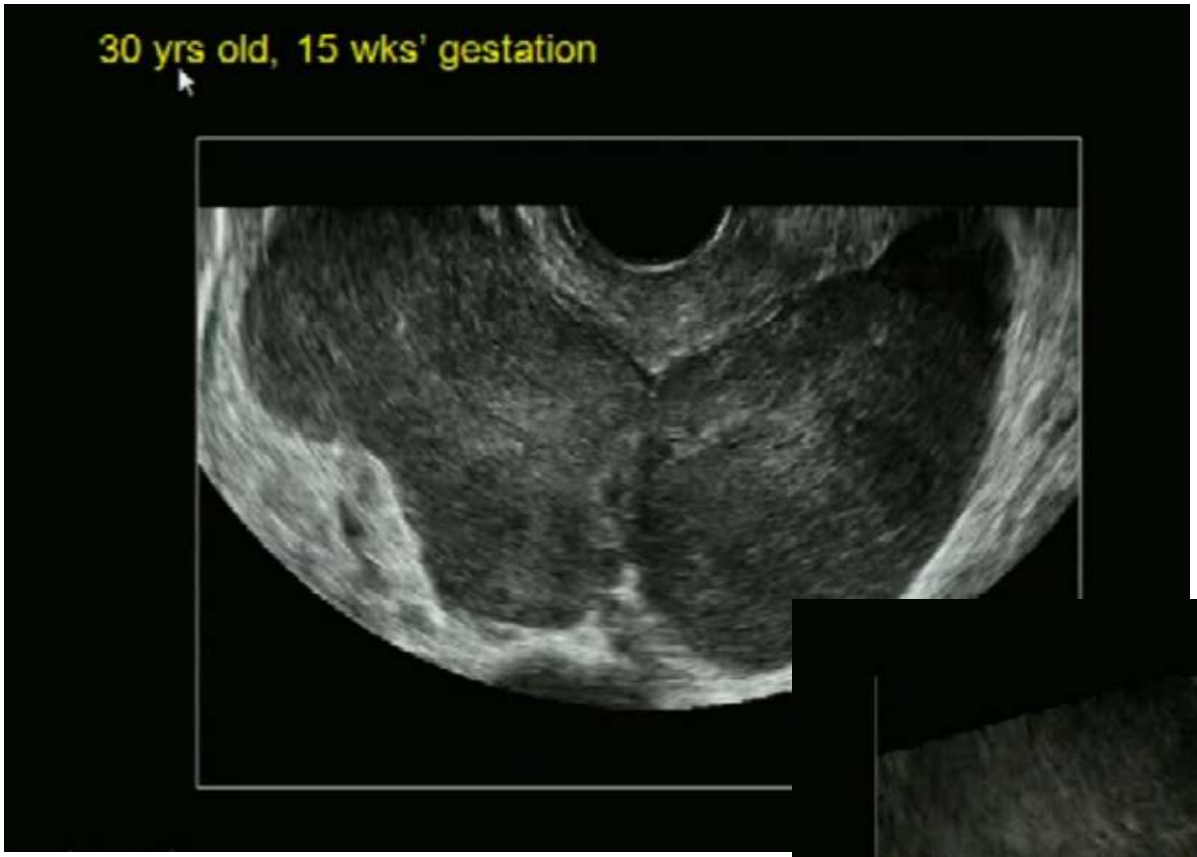
№2

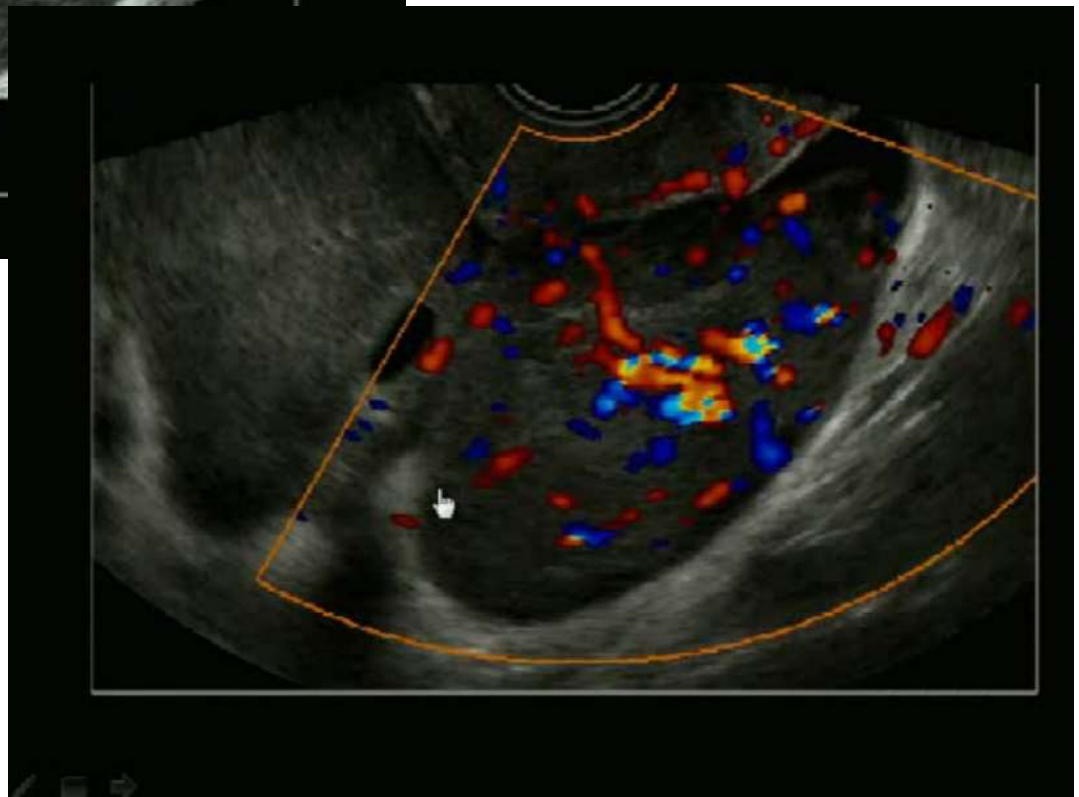


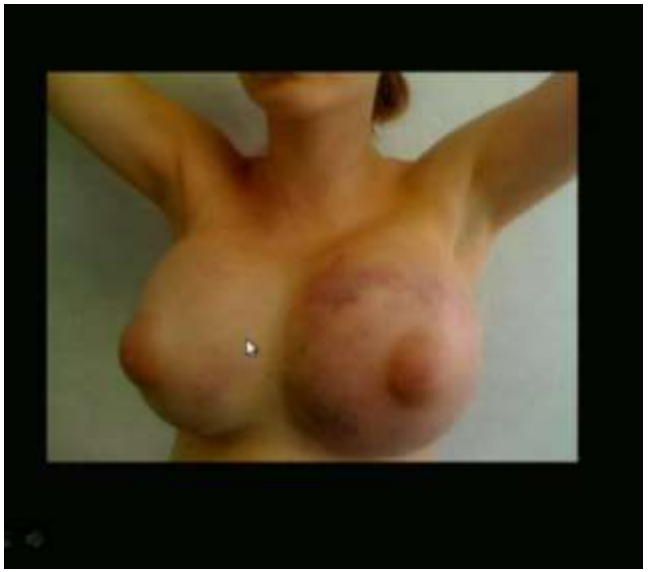


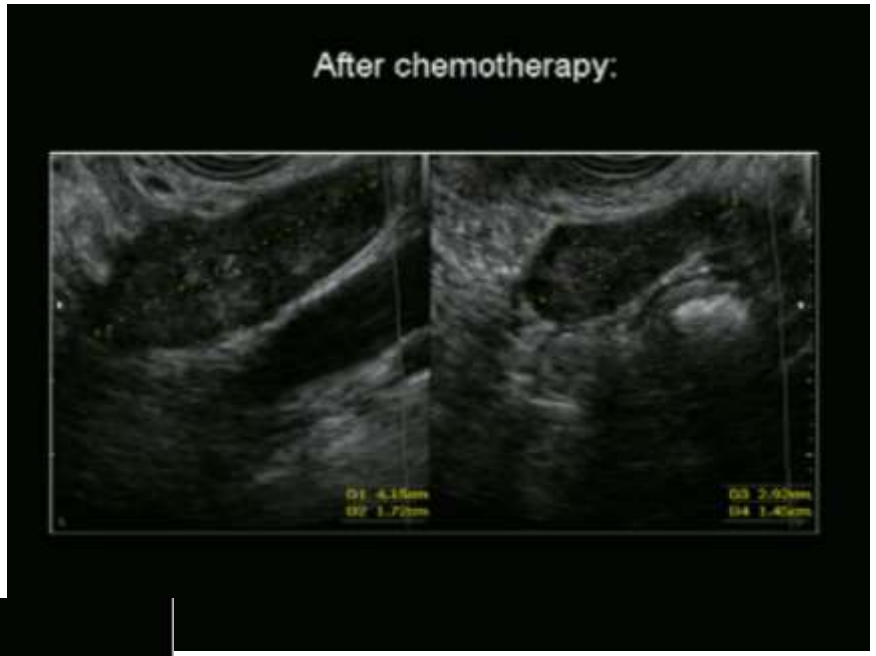
Однобічна пухлина. Пацієнтка на спостереженні після лікування лейкозу. Проведено біопсію. Виявився метастаз

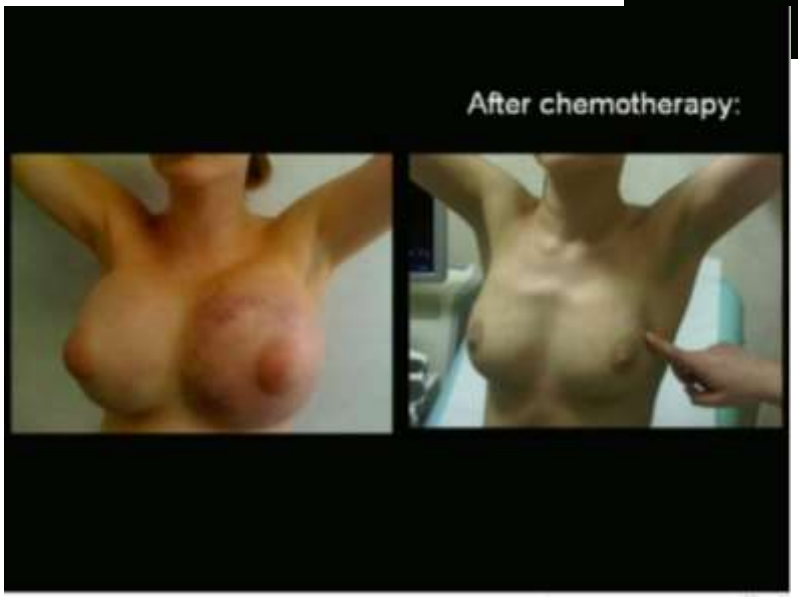
№3











Лімфома

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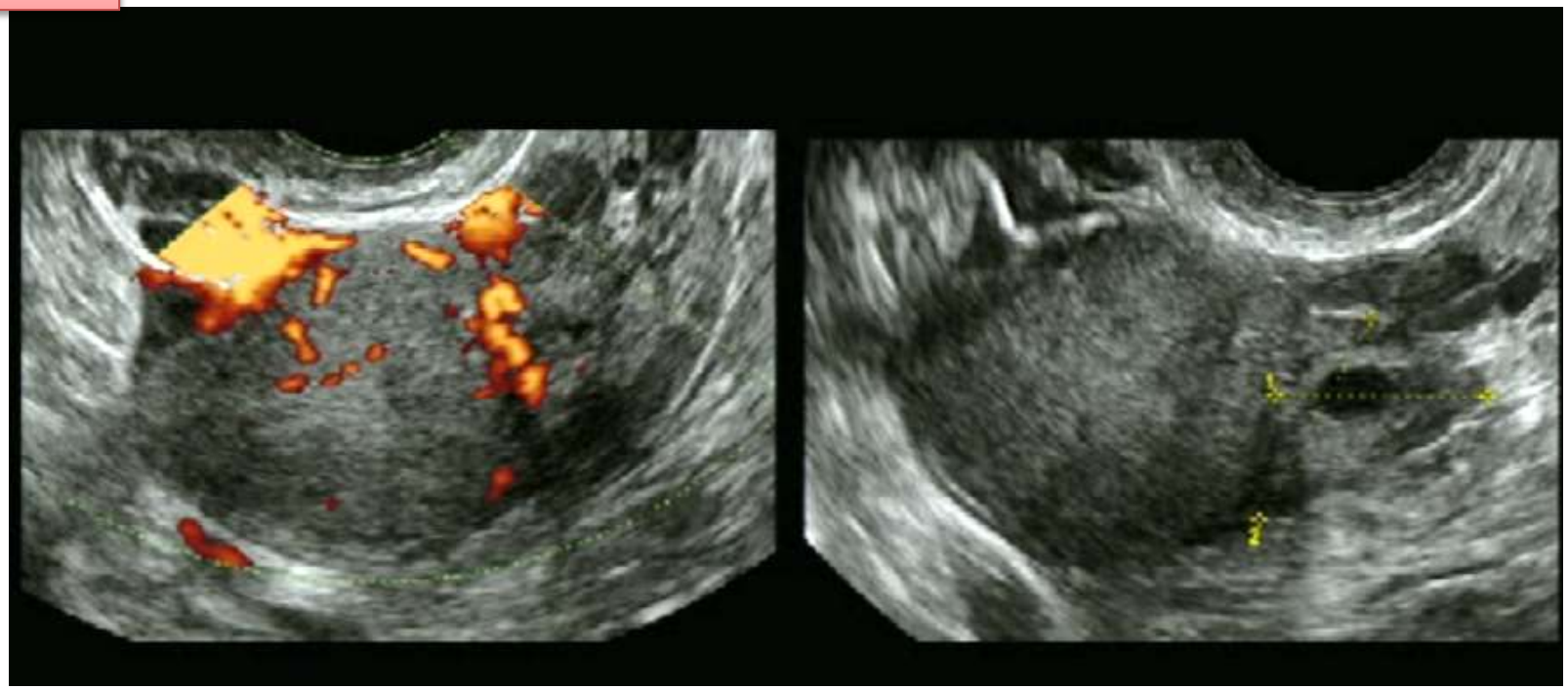

Однобічна пухлина. Фіброма? яєчника. Лікувалась з приводу карциноми легень.
Лапароскопія. Видалено пухлину.

Ovarian metatstasis from lung carcinoma

Ultrasonographic appearance of metastatic non-gynecological pelvic tumors

M. ZIKAN*, D. HSCHEROVA*, I. PINKAVOVA*, P. DUNDR† and D. CIBULA*

	"Crescent sign"
Colo-rectal	0/32
Upper gastrointestinal type	0/13
Lymphoma	11/11
Krukenberg tumor	0/9
Breast cancer	6/6

Ultrasound Obstet Gynecol 2012; 39: 219–225
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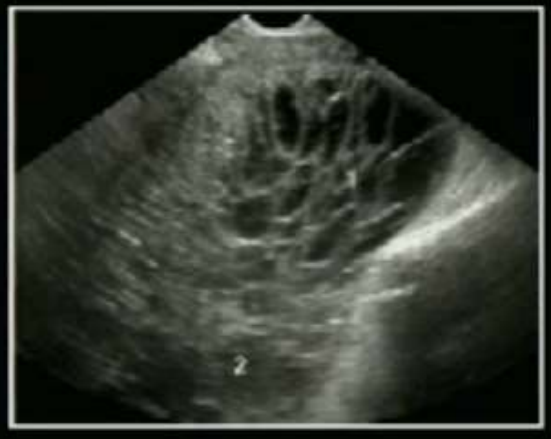
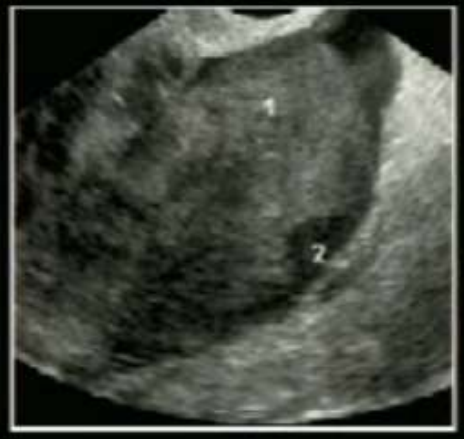
Ultrasonographic appearance of metastatic non-gynecological pelvic tumors

M. ZIKAN*, D. FISCHEROVA*, I. PINKAVOVA*, P. DUNDR† and D. CIBULA*

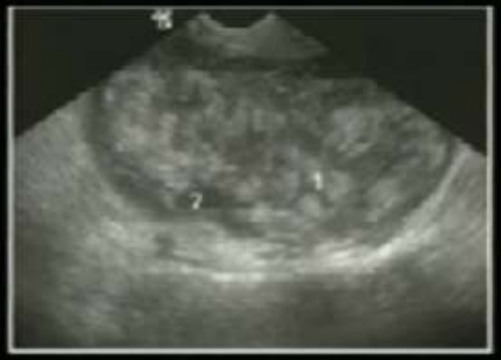
*Gynecologic Oncology Center, Department of Obstetrics and Gynecology, Charles University, Prague, First Medical Faculty and General Teaching Hospital, Prague, Czech Republic †Department of Pathology, Charles University, Prague, First Medical Faculty and General Teaching Hospital, Prague, Czech Republic



Biliary tract



Krukenberg



Lymphoma

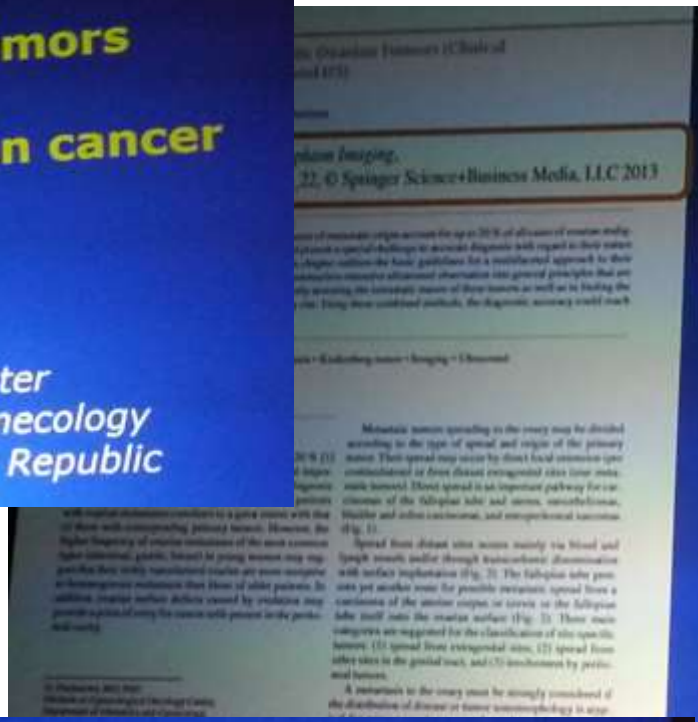
Висновки

- Характерно:
- 1. Двобічність
- 2. Щільна неоднорідна будова
- 3. Виразне судинне русло (дерево – проникаюча судина)
- Не характерно:
- 1. Папілярні розростання (але можливі)
- 2. Сліди незміненої яєчникової тканини (але можливі п)
- Важливо : анамнез (онкологія)!!!

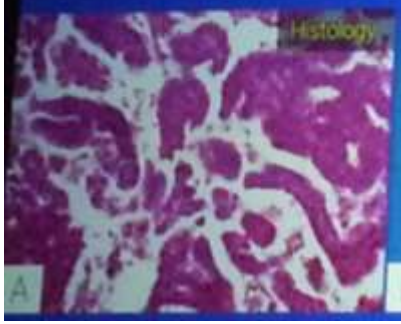
Non-gynecological tumors mimicking primary ovarian cancer

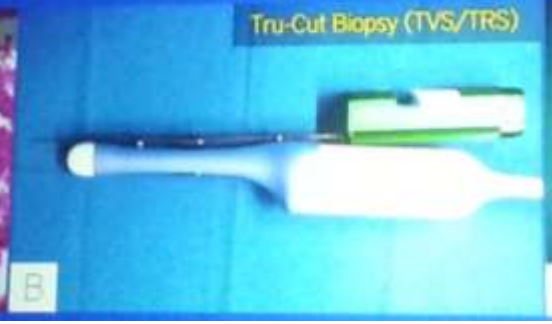
Fischerova Daniela

Gynecological Oncology Center
Department of Obstetrics and Gynecology
Charles University, Prague, Czech Republic



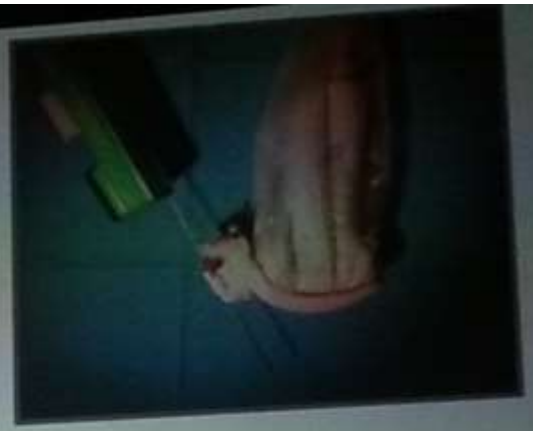
- Tru-Cut biopsy allows an adequate histological sample for timely initiation of an appropriate treatment *(Fischerova, Cibula et al. Int J Gynecol Cancer 2008)(Zikan, Fischerova et al. Ultrasound Obstet Gynecol 2010).*

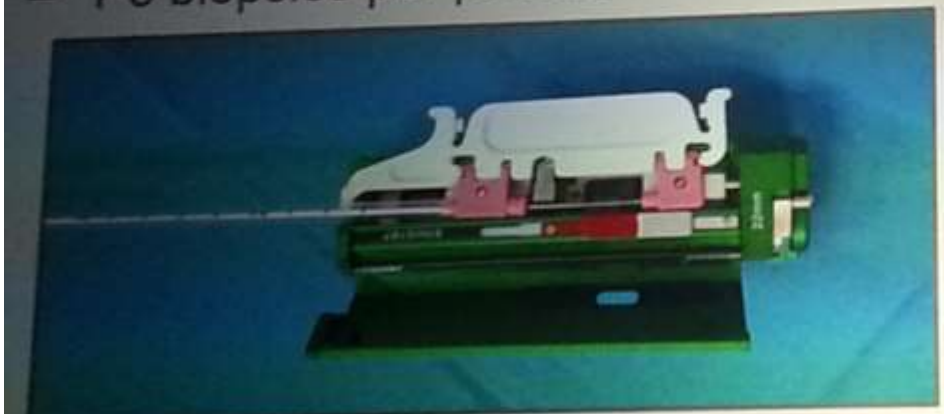




METHODS

- Bard biopsy Gun, 16-18G needle
- Biopsy route n (%):
  - Transvaginal 112 (91.1%),
  - transabdominal 9 (7.3%)
  - transrectal 2 (1.6%)
- 1-3 biopsies per patient





RESULTS

Complications moderate (hospital admission)

Abdominal wall hematoma (n=1)

Fever, pain – suspected infection (n=1)

RESULTS - Histological diagnosis according to true-cut biopsy (n=123)*

	Frequency n (%)
Conclusive diagnosis	**106/123 (86%)**
Ovarian cancer	74 (69.8%)
Non-ovarian malignancy	32 (30.1%)
Colorectal cancer	11 (10.3%)
Gastric cancer	7 (6.6%)
Breast cancer	4 (3.3
Lymphoma, Cervical-, pancreatic cancer	2 (1.9%)
GIST, Carcinoid, Sarcoma, Endometrial cancer	1 (0.9%)
Unknown primarity	**12 (9.8%)**
Non representative material	**5 (4.1%)**

* 33 women underwent cytoreductive surgery: histological diagnosis confirmed in **all** cases


Thank you for your
attention