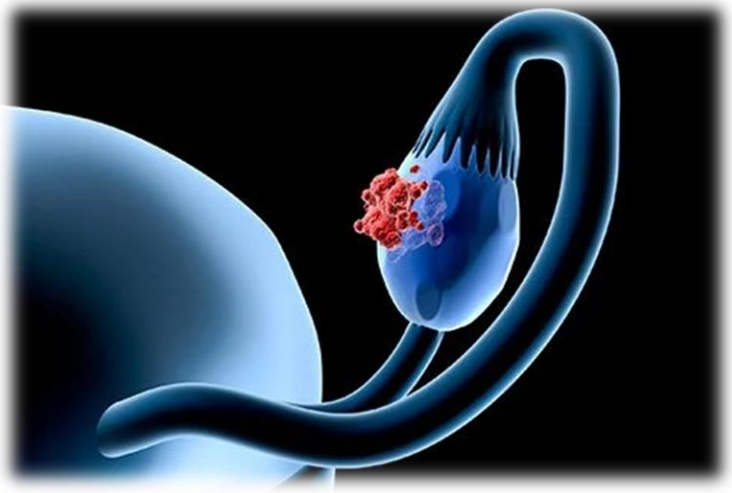
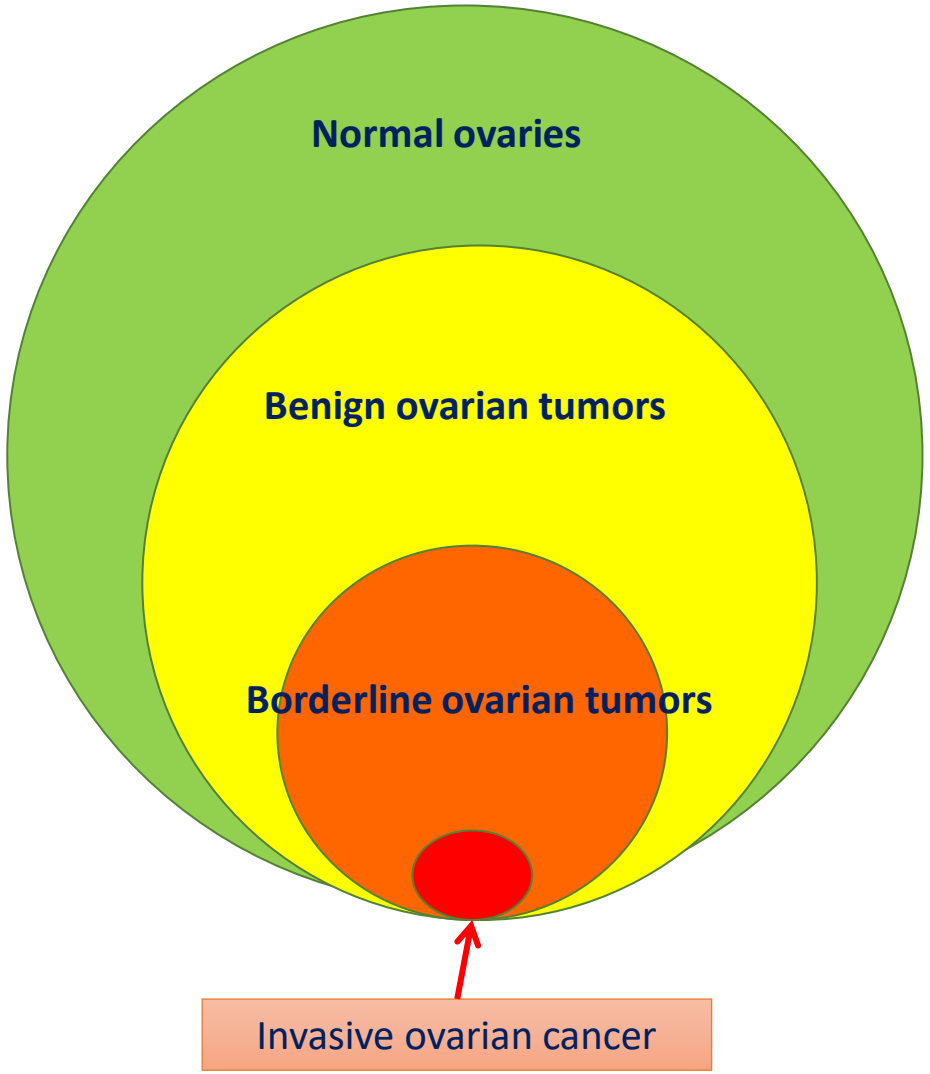
I tumori ovarici Borderline e Invasivi allo stadio iniziale



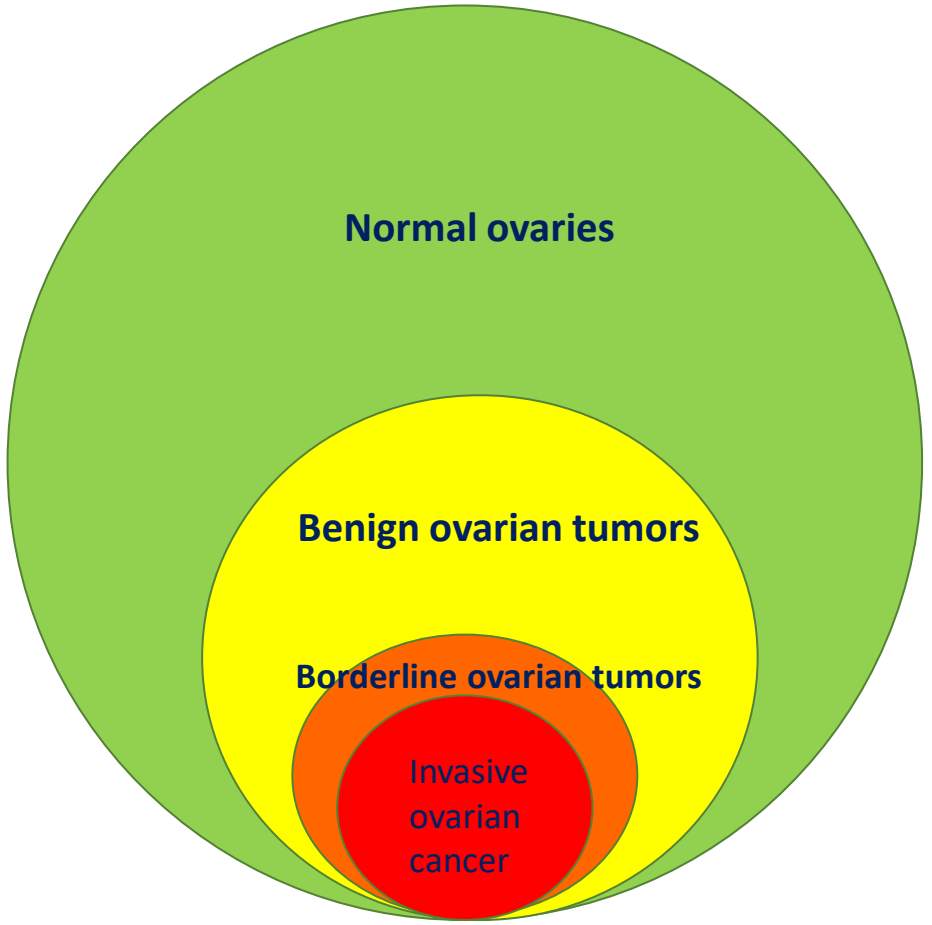
MILAN ULTRASOUND GYNECOLOGIC ONCOLOGY

Dorella Franchi
Preventive Gynecologic Unit
European Institute of Oncology

Fertile age



Post-menopause



ESGO/ISUOG/IOTA/ESGE Consensus Statement on pre-operative diagnosis of ovarian tumors

Dirk Timmerman [1,2] François Planchamp,[3] Tom Bourne [1,2,4] Chiara Landolfo [5]
Andreas du Bois,[6] Luis Chiva [7] David Cibula [8] Nicole Concin [6,9] Daniela Fischerova [8]
Wouter Froyman [1] Guillermo Gallardo Madueño [10] Birthe Lemley,[11,12] Annika Loft,[13]
Liliana Mereu,[14] Philippe Morice,[15] Denis Querleu [16,17] Antonia Carla Testa [5,18]
Ignace Vergote,[19] Vincent Vandecaveye [20,21] Giovanni Scambia,[5,18] Christina Fotopoulou [22]

isuog.org

CONSENSUS STATEMENT

ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumors

UOG 2021

1. **Subjective assessment by expert** (Level-III) ultrasound examiners has the best performance to distinguish between benign and malignant ovarian tumors.
– Level of evidence: 1a
– Grade of statement: A

2. If an expert ultrasound examiner is not available, the use of **ultrasound-based diagnostic models** can assist clinicians to distinguish between benign and malignant ovarian tumors.
– Level of evidence: 2a
– Grade of statement: B

IOTA models:
- Easy descriptors
- Simple Rules/SRR
- ADNEX
- O-RADS

ESGO/ISUOG/IOTA/ESGE Consensus Statement on pre-operative diagnosis of ovarian tumors

Dirk Timmerman [1,2] François Planchamp,[3] Tom Bourne [1,2,4] Chiara Landolfo [5]
Andreas du Bois,[6] Luis Chiva [7] David Cibula [8] Nicole Concin [6,9] Daniela Fischerova [8]
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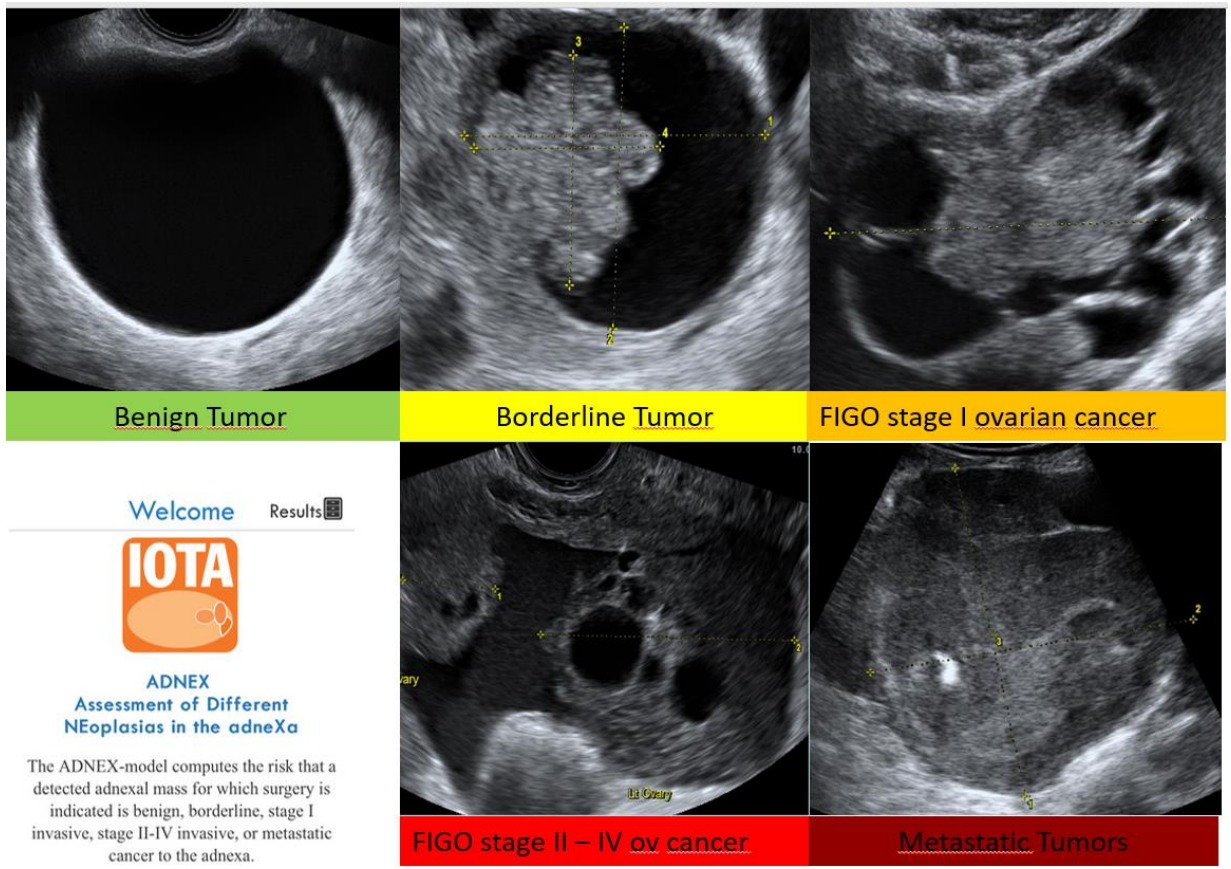
CONSENSUS STATEMENT

ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumors

UOG 2021

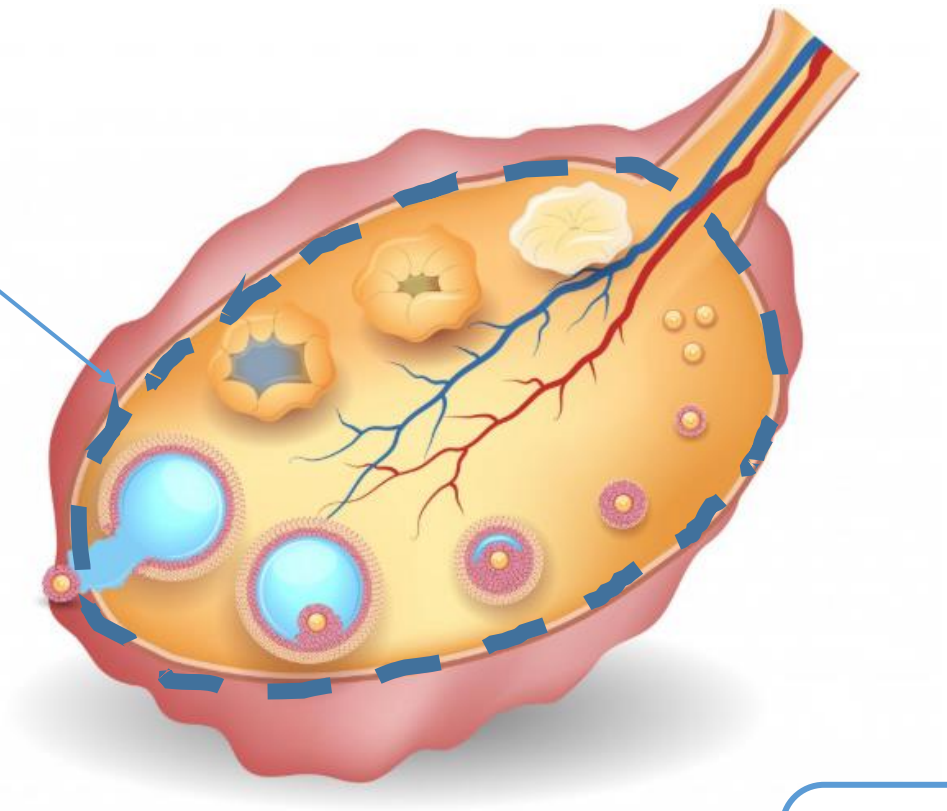
5. The **IOTA ADNEX model** is a multiclass model and is helpful to differentiate between benign tumors, borderline tumors, early- or advanced-stage ovarian cancer and secondary metastatic tumors.
– Level of evidence: 3b
– Grade of statement: C



FERTILE AGE

Malignant ovarian tumors

Epithelial
Ovarian tumors

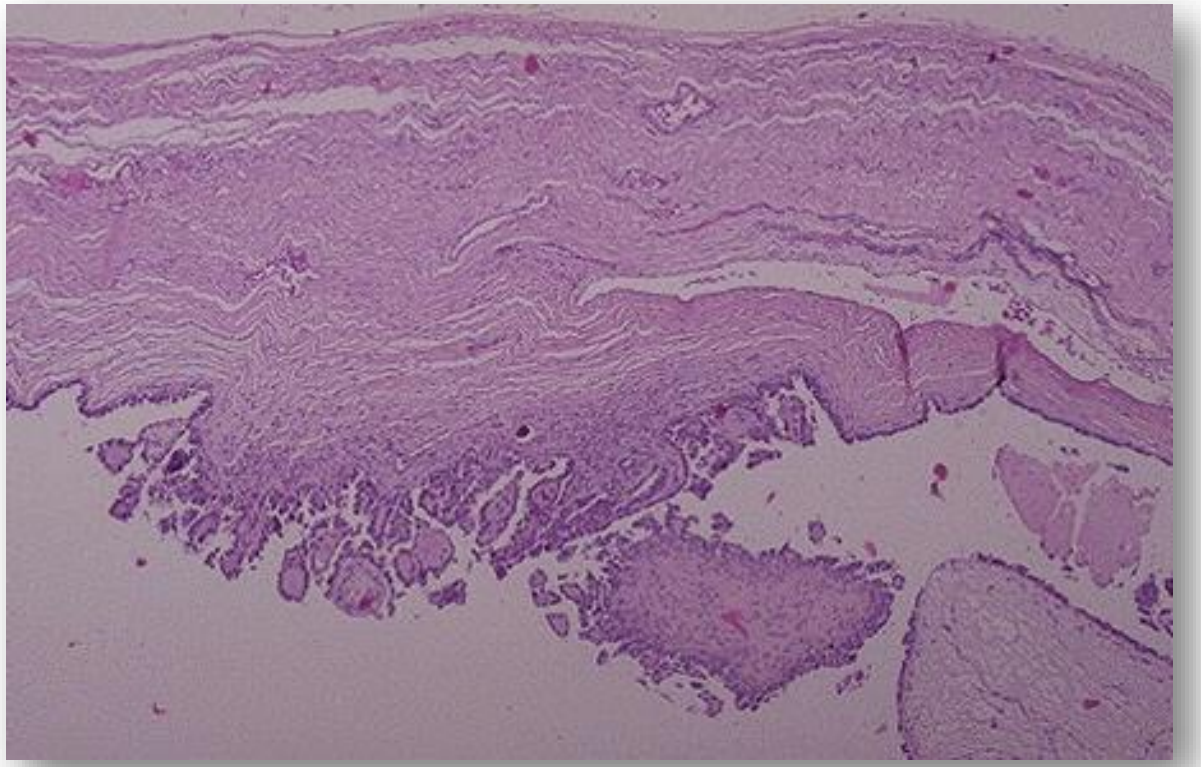


BOT Tumors

Primary Invasive tumors

BOTs - Definition

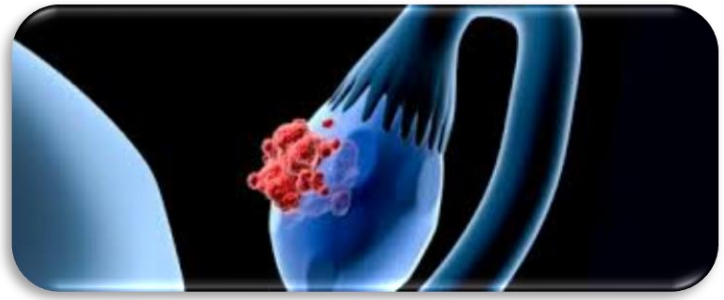
Epithelial ovarian tumors with histologic and biologic features intermediate between clearly benign and clearly malignant ovarian neoplasms.
The malignant cells do not invade the stroma of the ovary

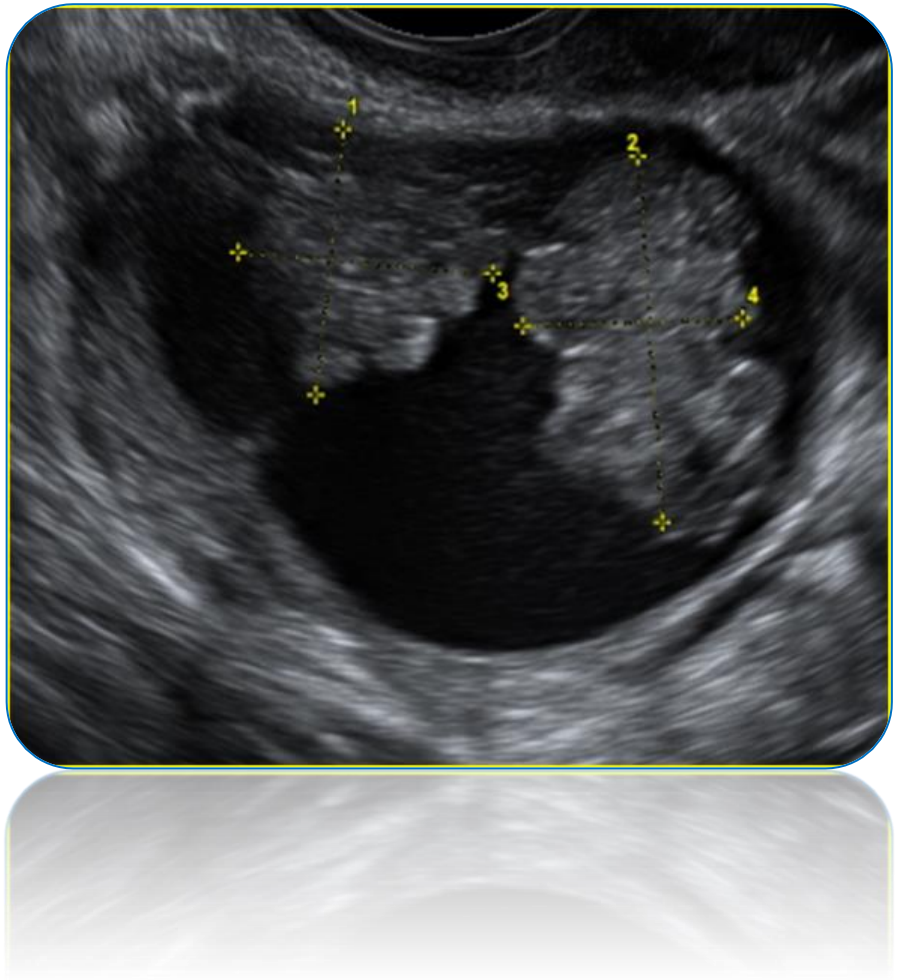


Microinvasion (<5 mm) can be seen in borderline tumours but these cases should still be regarded as borderline for classification and management purposes

ESMO–ESGO consensus conference recommendations on ovarian cancer. Annals of Oncology 2019

Borderline Ovarian Tumors





- 10-15% Of all ovarian tumors
- 50-80% Stage I
- 35% of patients < 40 yrs
- 99% Five years Ov Surv stage I
- 85-92% Five years Ov Surv > stage I
- Fertility sparing surgery

BOTs – Histological Classification

	Prevalence
Serous	50-60%
Mucinous Endocervical Type Intestinal Type	35% (15%) (85%)
Others Endometrioid Clear Cells Brenner tumor	4-8%

Ultrasound Obstet Gynecol 2005; 26: 644–650
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.2607

Ultrasound features of different histopathological subtypes of borderline ovarian tumors

E. FRUSCELLA*, A. C. TESTA*, G. FERRANDINA*, F. DE SMET†, C. VAN HOLSBEKE‡, G. SCAMBIA§, G. F. ZANNONI¶, M. LUDOVISI*, R. ACHTEN**, F. AMANT‡, I. VERGOTE‡ and D. TIMMERMAN‡

Educational video lecture

Ultrasound, macroscopic and histological features of borderline ovarian tumors

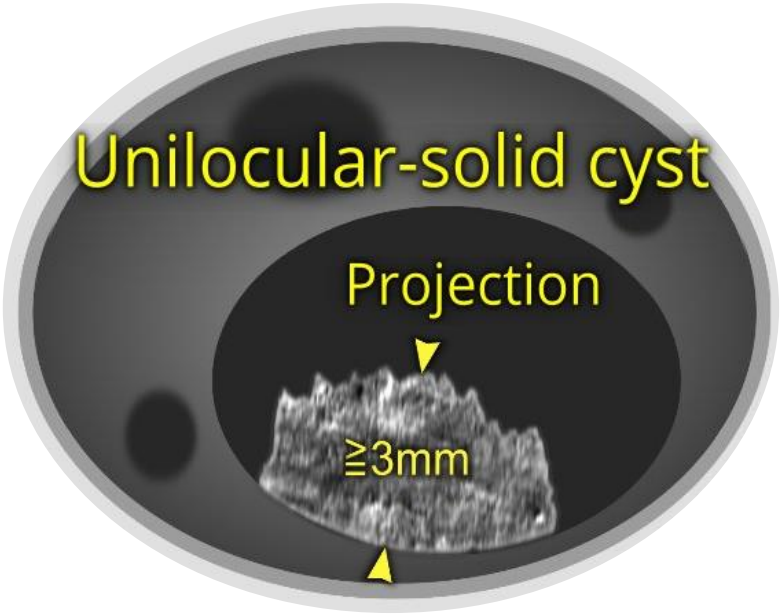
Valeria Verdecchia, Paola Romeo, Damiano Arciuolo, Francesca Moro

Serous Borderline Tumors

Mucinous Endocervical Type

Common morphological features

Morphological features suggestive of serous type or endocervical type BOT

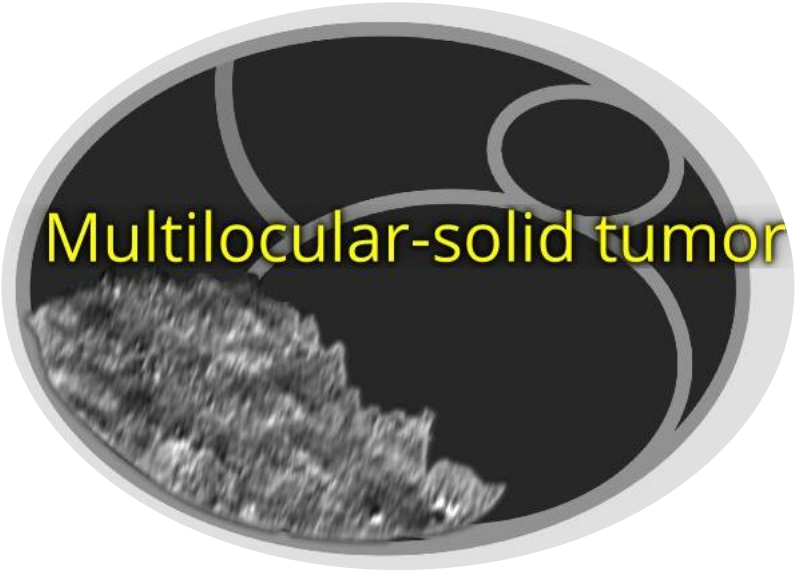


Unilocular-solid Cysts BOT

42% (serous) 48% (endocervical)

Fruscella E. Testa A.C. et al. Ultrasound Obstet Gynecol 2005

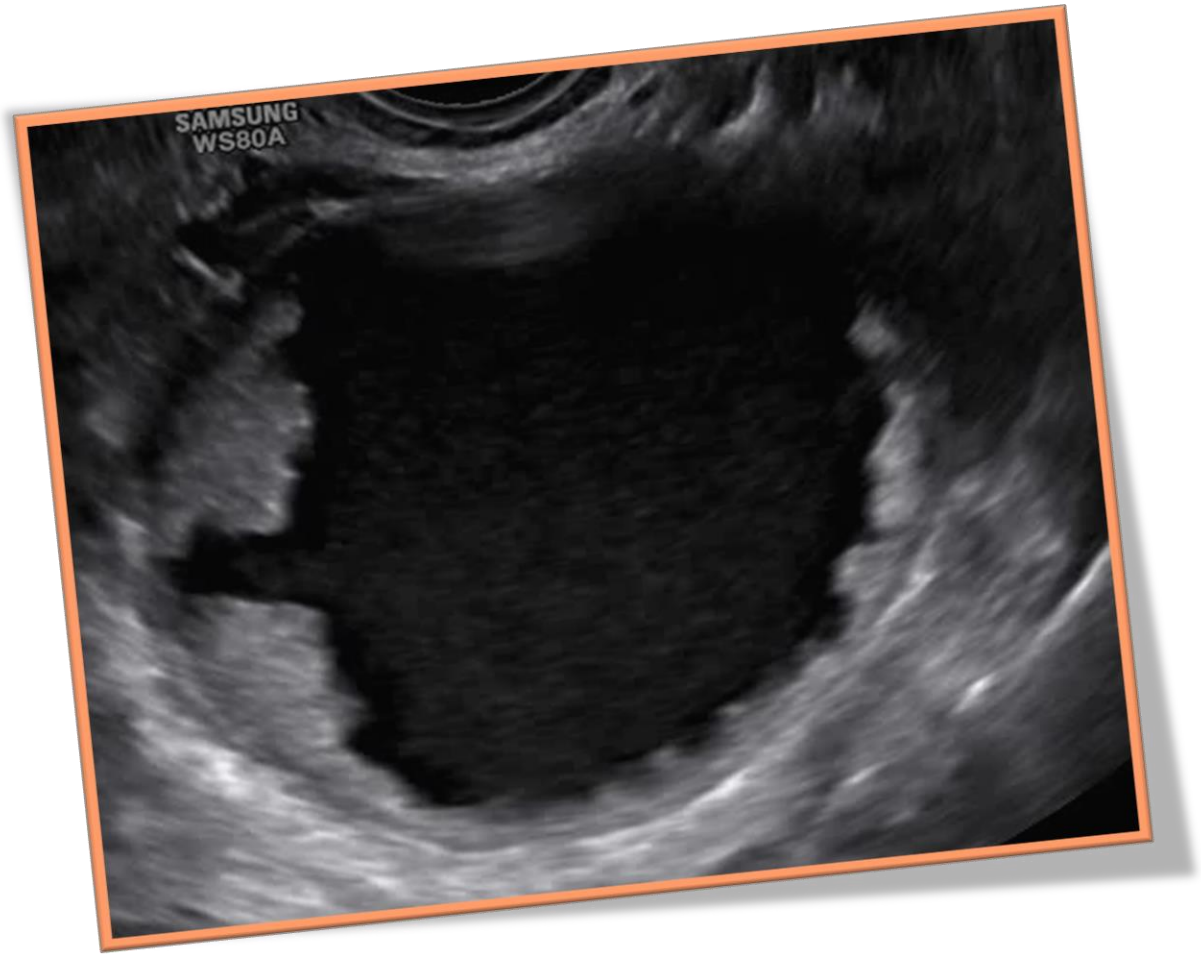
Morphological features suggestive of serous type or endocervical type BOT



Multilocular-solid Cysts BOT

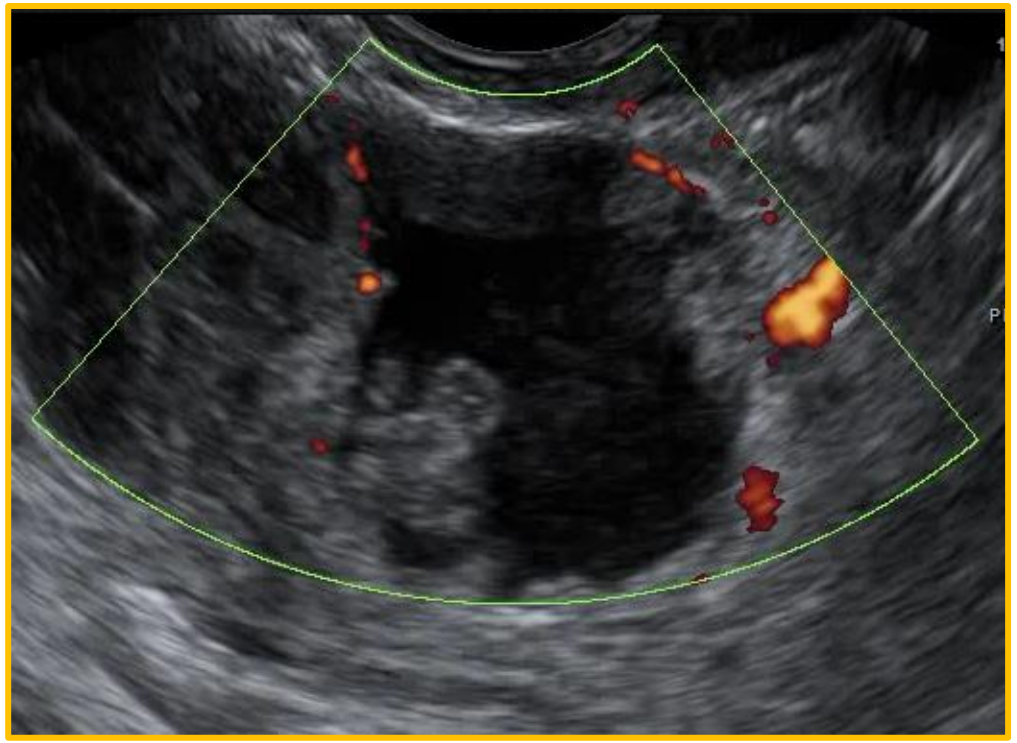
38% (serous) 26% (endocervical)

Morphological features suggestive of serous type or endocervical type BOT



Multiple papillary projection

82% (serous) 74% (endocervical)



Papillary projections

FRAGILE

New sonographic marker of borderline ovarian tumor: microcystic pattern of papillae and solid components

UOG 2019

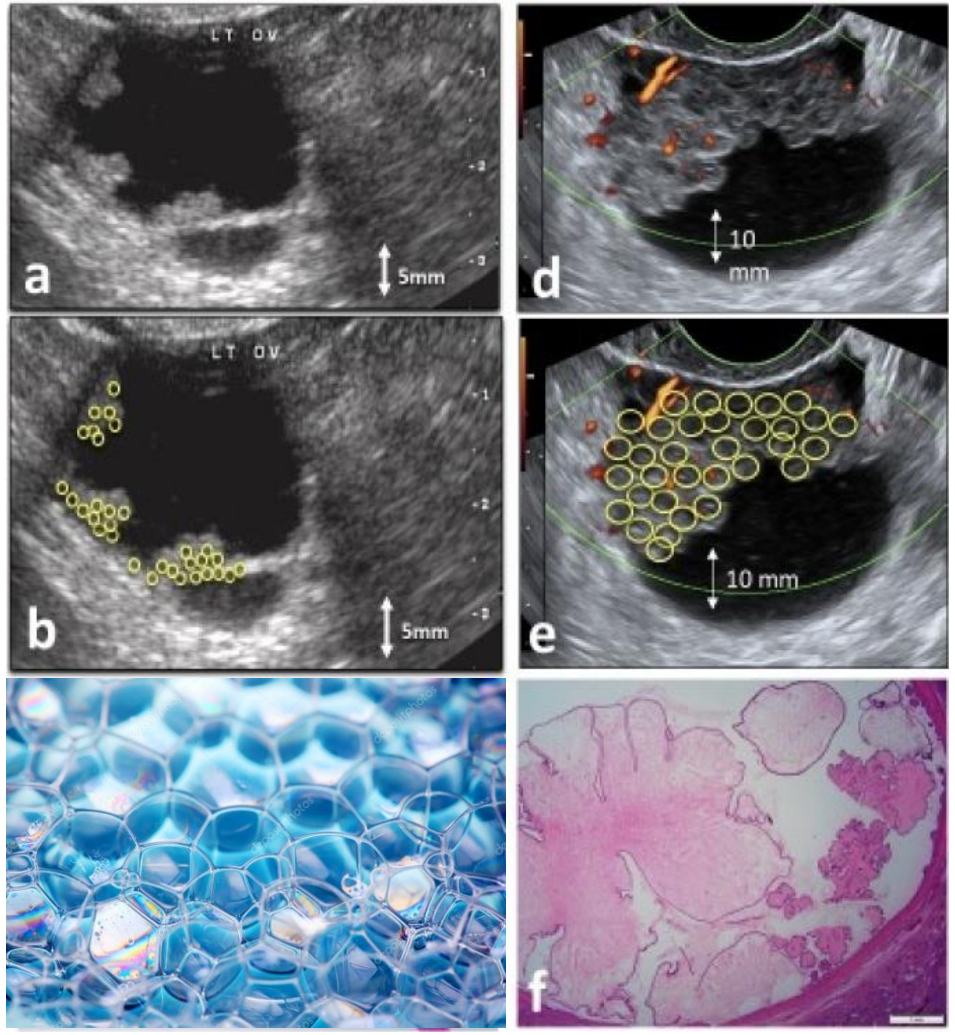
I. E. TIMOR-TRITSCH[1], C. E. FOLEY[1], C. BRANDON[1], E. YOON[2], J. CIAFFARRANO[2], A. MONTEAGUDO[3], K. MITTAL[2] and L. BOYD[4]

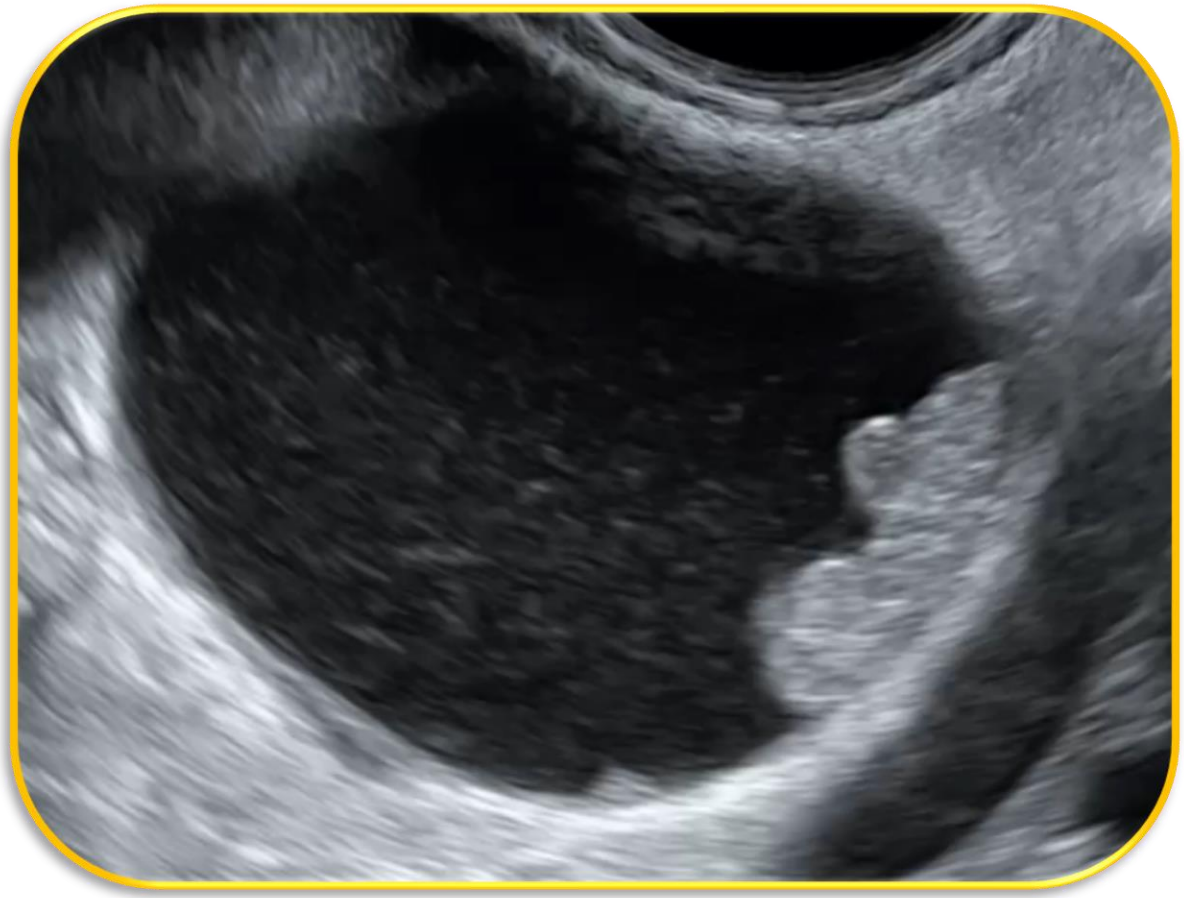
Retrospective study

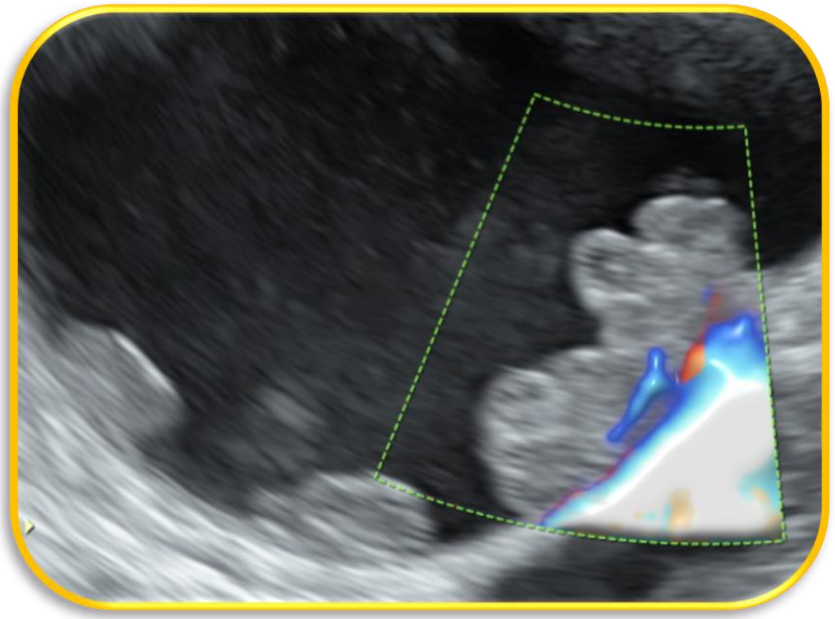
60/67 (89.7%) BOTs demonstrated a microcystic pattern

- *The microcystic appearance was defined as: presence of thin walled, fluid filled (anechoic or low-level), cluster(s) of 1-3 mm in either small or large areas.*
- *Usually located along the inner cyst wall with papillae or a solid component, but can also straddle septa*

They appear as Loosely and randomly piled miniature bubbles, resembling agitated soapy water



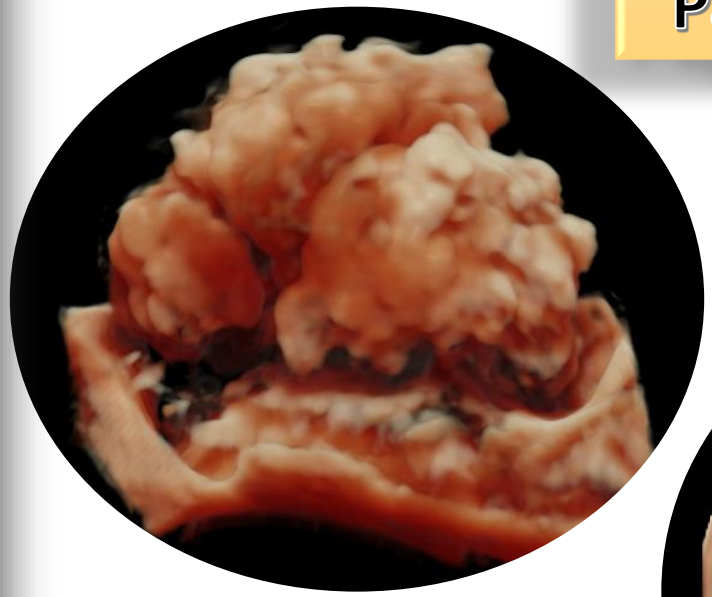


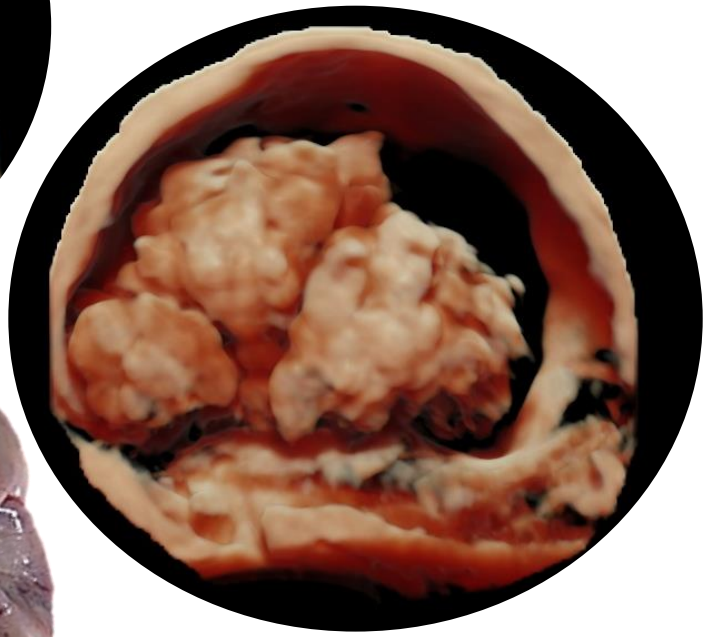


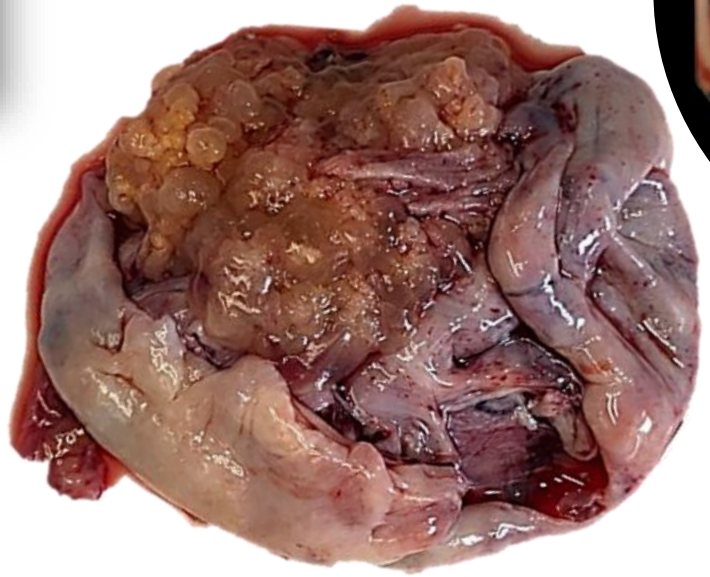
Numerous and disseminated

Serous BOT Stage IA

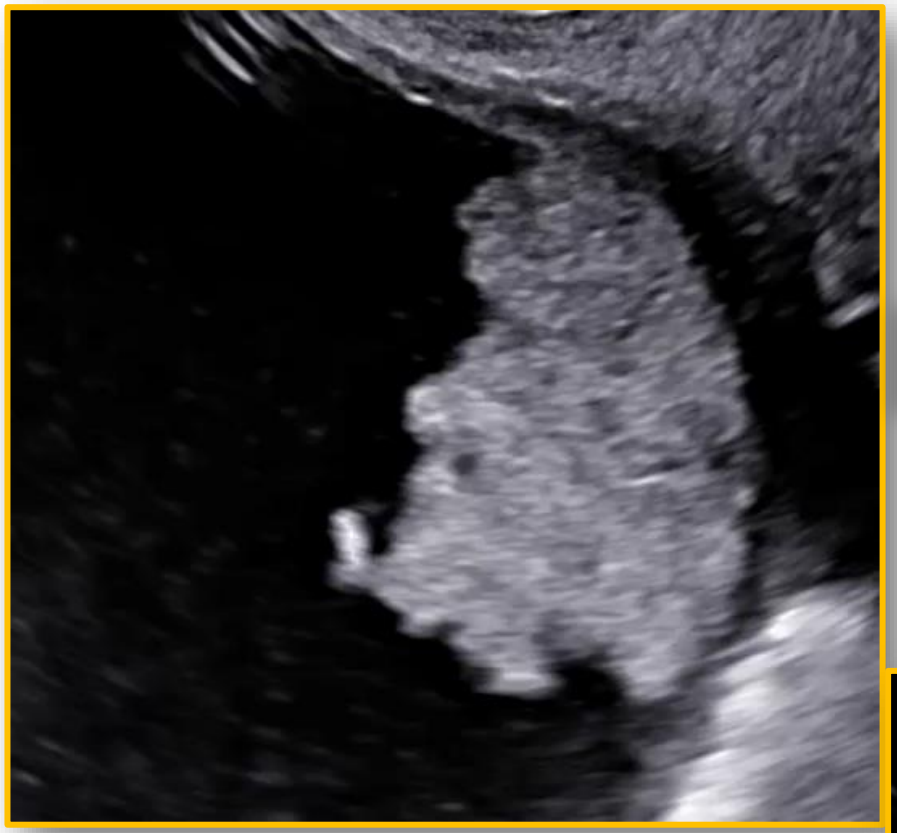
Confluent
Papillary projection



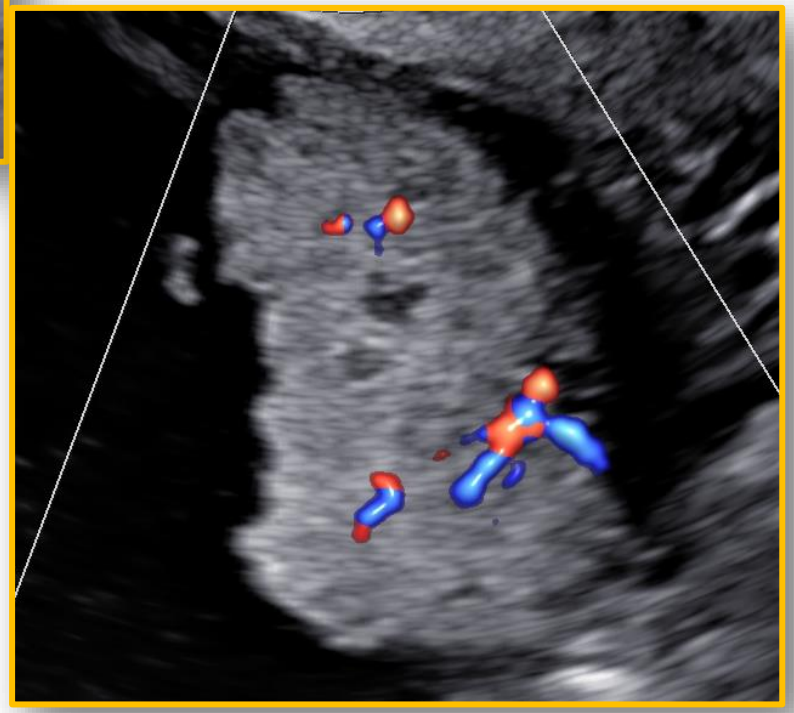




Serous BOT stage IA

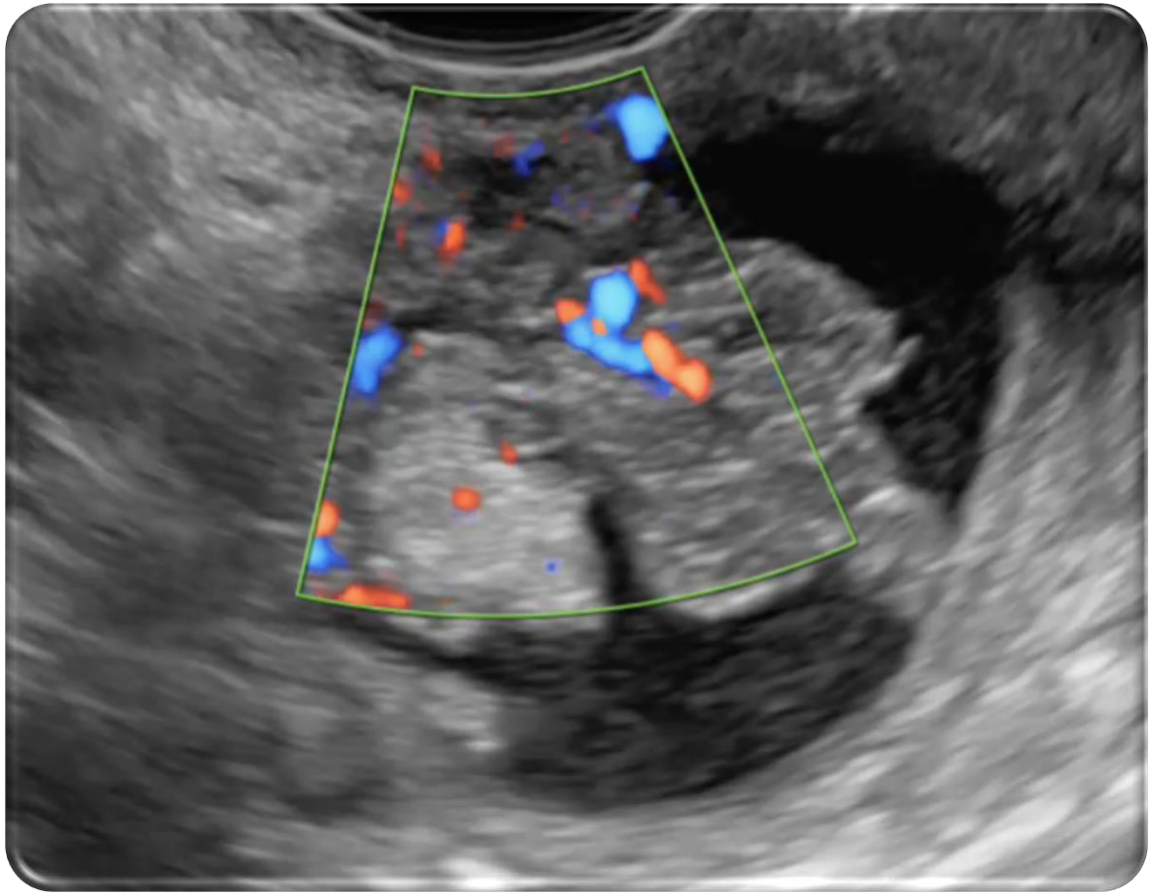


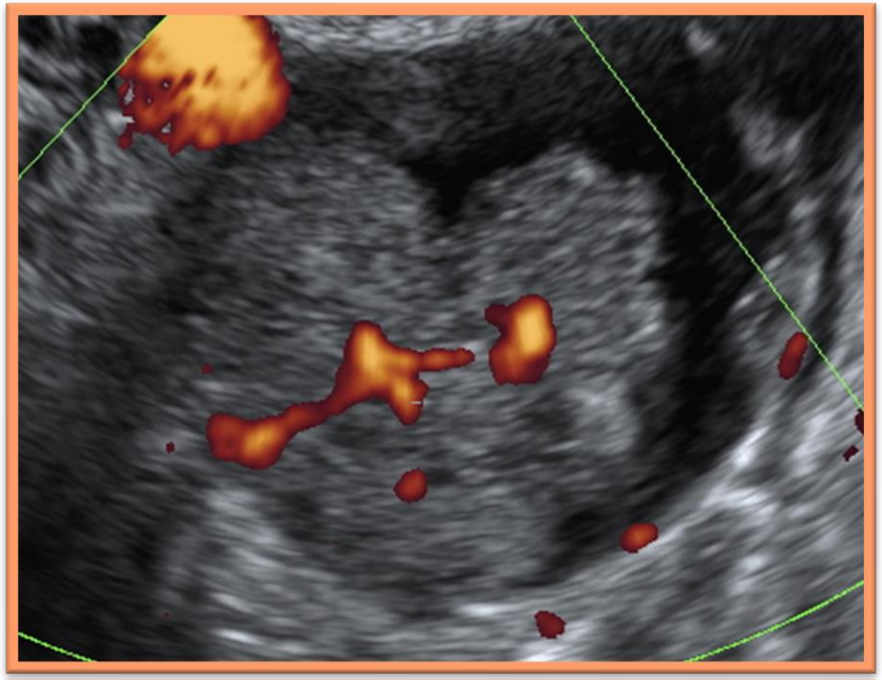
Papillary Projections

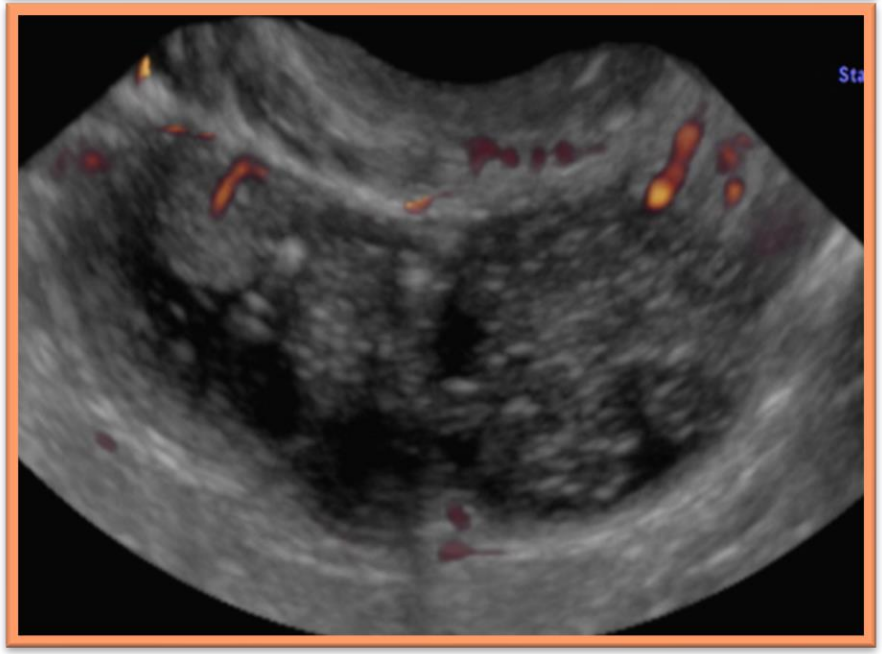


Irregular contour

Papillary projections







Vascularization on CD or PD (80%)
CS 2-3

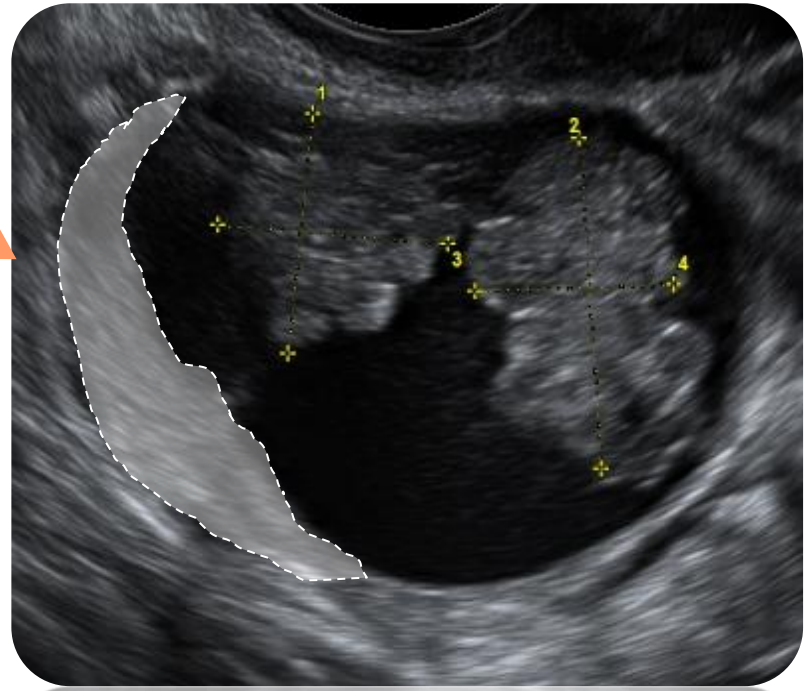
Ultrasound Obstet Gynecol 2007; 29: 489–495
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.4002

Accuracy of ultrasound subjective 'pattern recognition' for the diagnosis of borderline ovarian tumors

J. YAZBEK*, K. S. RAJU†, J. BEN-NAGI*, T. HOLLAND*, K. HILLABY* and D. JURKOVIC*

Morphological features suggestive of serous type or endocervical type BOT

Ovarian Crescent sign



Ultrasound Obstet Gynecol 2018; 52: 269–278
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.18951

Differences in ultrasound features of papillations in unilocular-solid adnexal cysts: a retrospective international multicenter study

C. LANDOLFO[1,2], L. VALENTIN[3], D. FRANCHI[4], C. VAN HOLSBEKE[5], R. FRUSCIO[6], W. FROYMAN[1,2], P. SLADKEVICIUS[3], J. KAIJSER[7], L. AMEYE[1], T. BOURNE[1,2,8], L. SAVELLI[9], A. COOSEMANS[2,10], A. TESTA[11] and D. TIMMERMAN[1,2]

204 masses

RETROSPECTIVE STUDY

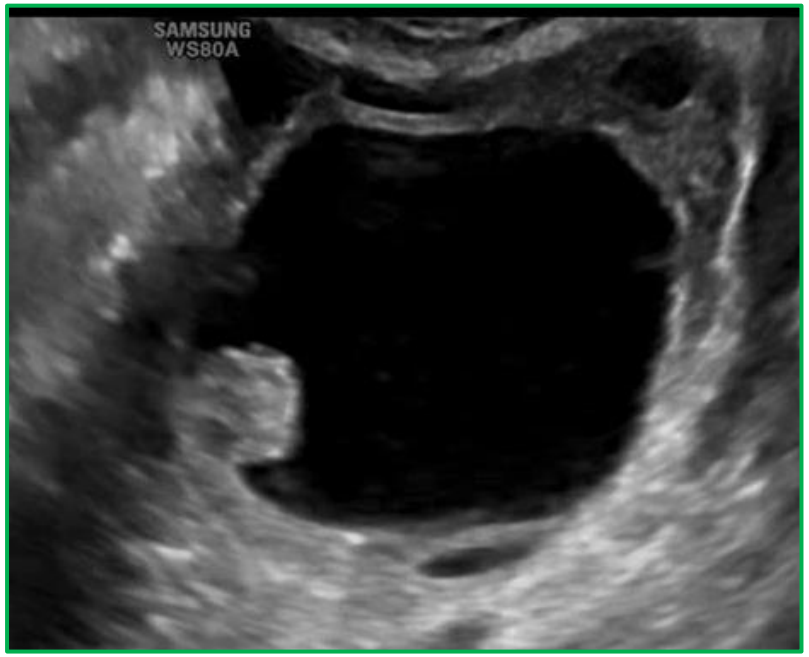
- ✓ Large and numerous (disseminated) papillations
- ✓ Confluent papillations
- ✓ Vascularization on color or PD
- ✓ Anechoic spaces

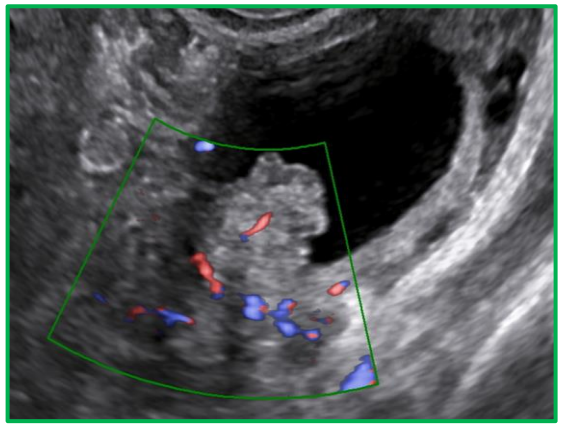
↑ **the risk of malignancy**

- ✓ Shadows behind hyperechoic foci in the papillations or in the cyst
- ✓ Shadows behind the papillations themselves

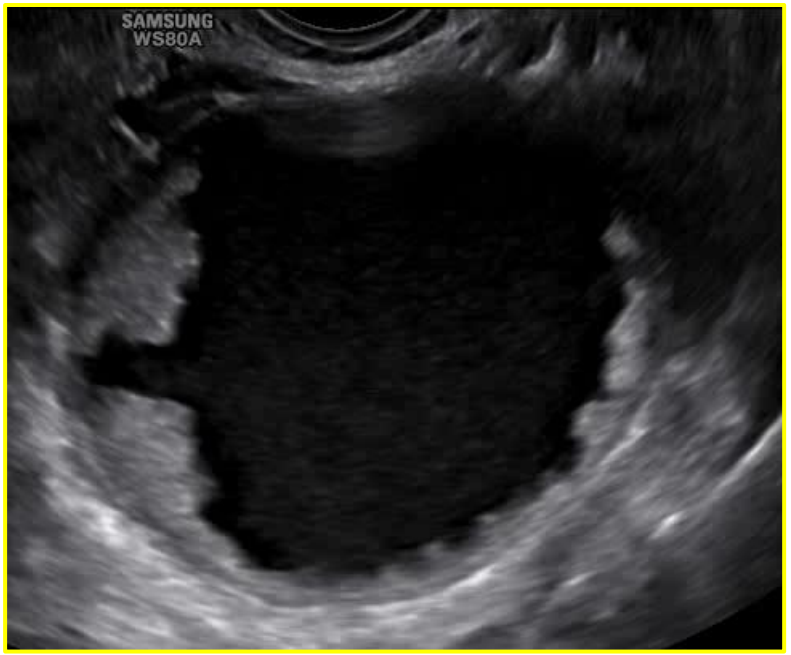
↓ **the risk of malignancy**

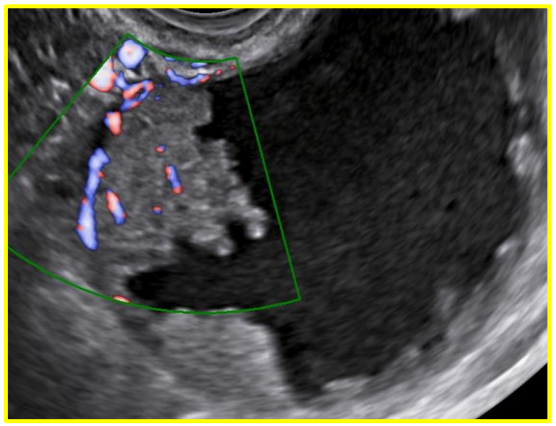
Variable	*Benign (n = 131)*	*Borderline (n = 42)*	*Primary invasive and metastasis (n = 31)*
Number of papillations			
1	84 (64)	16 (38)	7 (23)
2	14 (11)	1 (2)	4 (13)
3	15 (11)	5 (12)	3 (10)
> 3	18 (14)	20 (48)	17 (55)
Height of largest papillation (mm)			
Mean ± SD	10 ± 7	16 ± 10	24 ± 14
Median (range)	7 (3–44)	14 (7–60)	20 (4–54)
Flow inside at least one papillation	36 (27)	34 (81)	29 (94)
Irregular contour in at least one papillation	81 (62)	39 (93)	26 (84)
Papillary dissemination			
< 25%	96 (73)	6 (14)	10 (32)
25–50%	27 (21)	21 (50)	9 (29)
> 50%	8 (6)	15 (36)	12 (39)
Papillary angle			
< 90%	28 (21)	8 (19)	1 (3)
≥ 90%	12 (9)	1 (2)	4 (13)
Both < 90° and ≥ 90° in same cyst	91 (69)	33 (79)	26 (84)
Acoustic shadows behind at least one papillation	37 (28)	1 (2)	3 (10)
Anechoic spaces inside at least one papillation	31 (24)	26 (62)	18 (58)
At least one hyperechoic papillation	45 (34)	5 (12)	9 (29)
Hyperechoic focus with acoustic shadows in papillations or in cyst wall	12 (9)	0 (0)	0 (0)
Confluent papillations	9 (7)	22 (52)	14 (45)



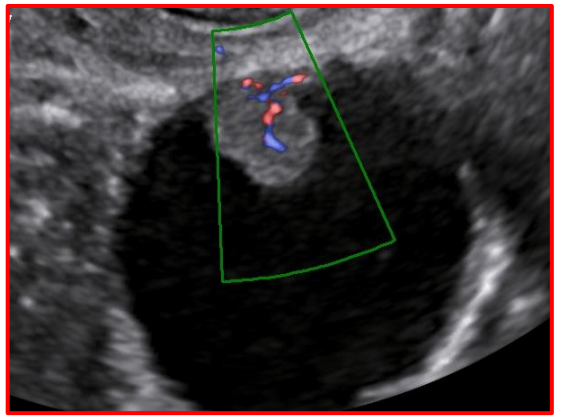


Benign

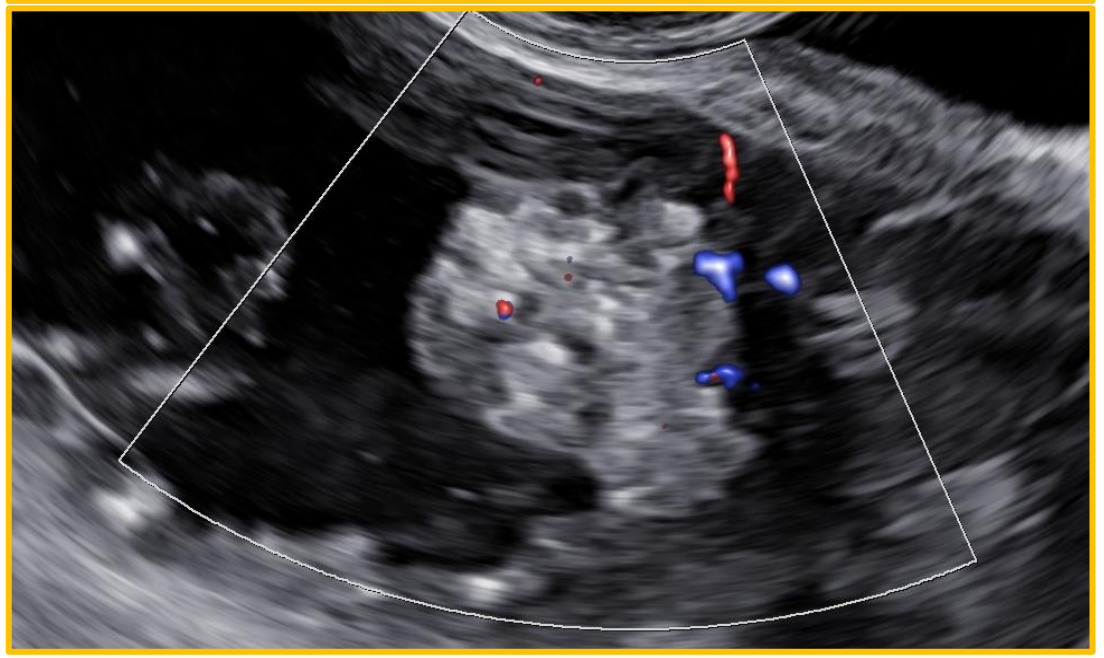




Borderline



Malignant



14 yrs

Serous BOT stage IA
multiple microinvasive foci (2-3 mm)

Can BOT tumors appear as solid tumors?

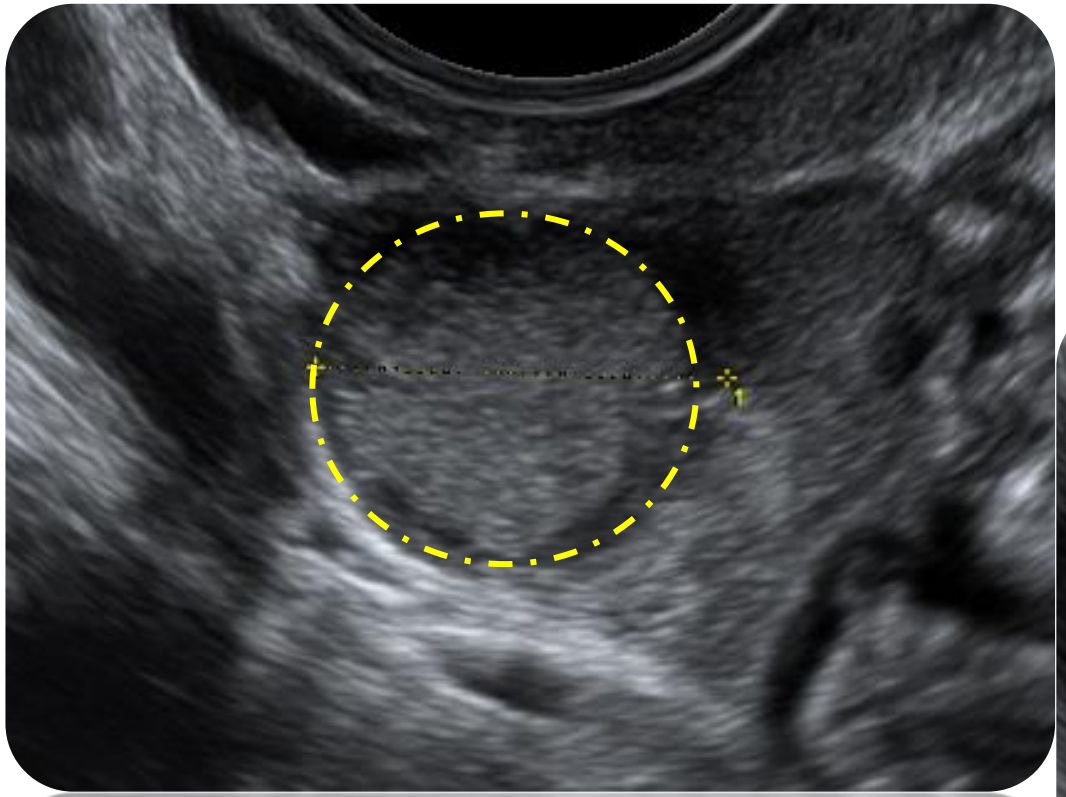
Ultrasound findings in 406 pts with serous ovarian tumors

	BOT	Non invasive LG	Invasive LG	High Grade
Patients	**64**	11	31	300
Morfology				
Unilocular	1 (1.6)	0	1 (3.2)	0
Unilocular-solid	**35 (54.7)**	4 (36.4)	3 (9.7)	8
Multilocular	2 (3.1)	0	0	2
Multilocular-solid	19 (29.7)	7 (63.6)	17 (54.8)	98 (32.6)
Solid	7 (10.9)	0	10 (32.2)	192 (63.9)
Largest diameter of the largest solid component	**26**	27	50	63
Presence of papillae	**52 (81)**	9 (81)	10 (32)	21 (7)
Hyperechoic foci present	**6 (9)**	1 (9)	12 (34)	5 (1)
Ovarian crescent sign	**22 (34)**	1(9)	6 (19)	3(1)

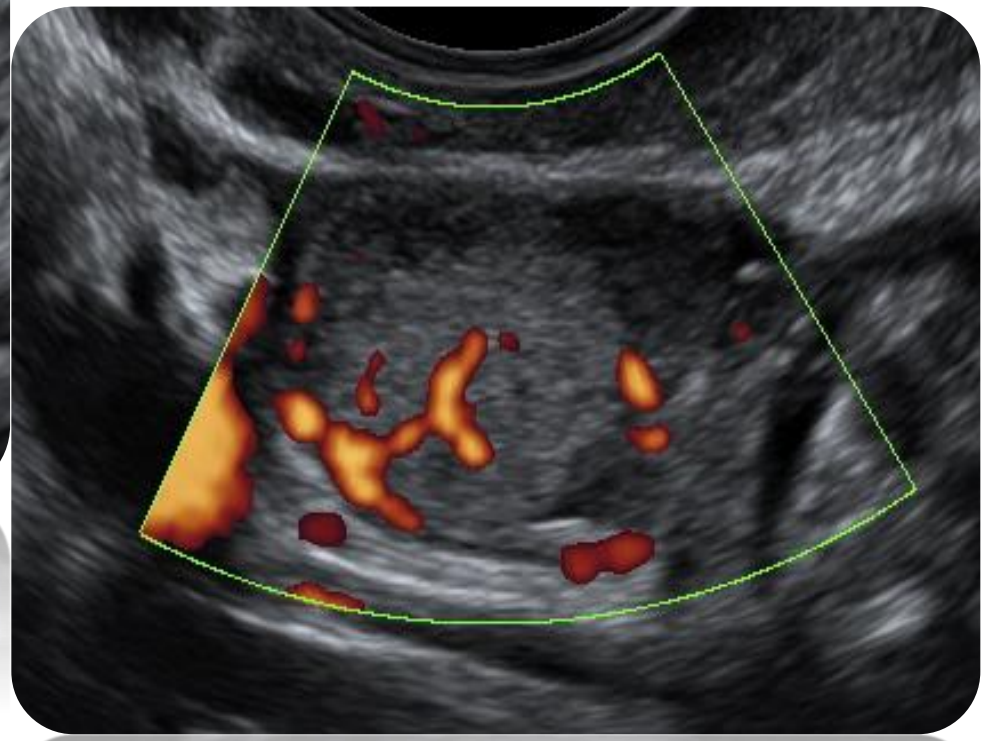
F. Moro et al. UOG 2017

IEO Istituto Europeo di Oncologia

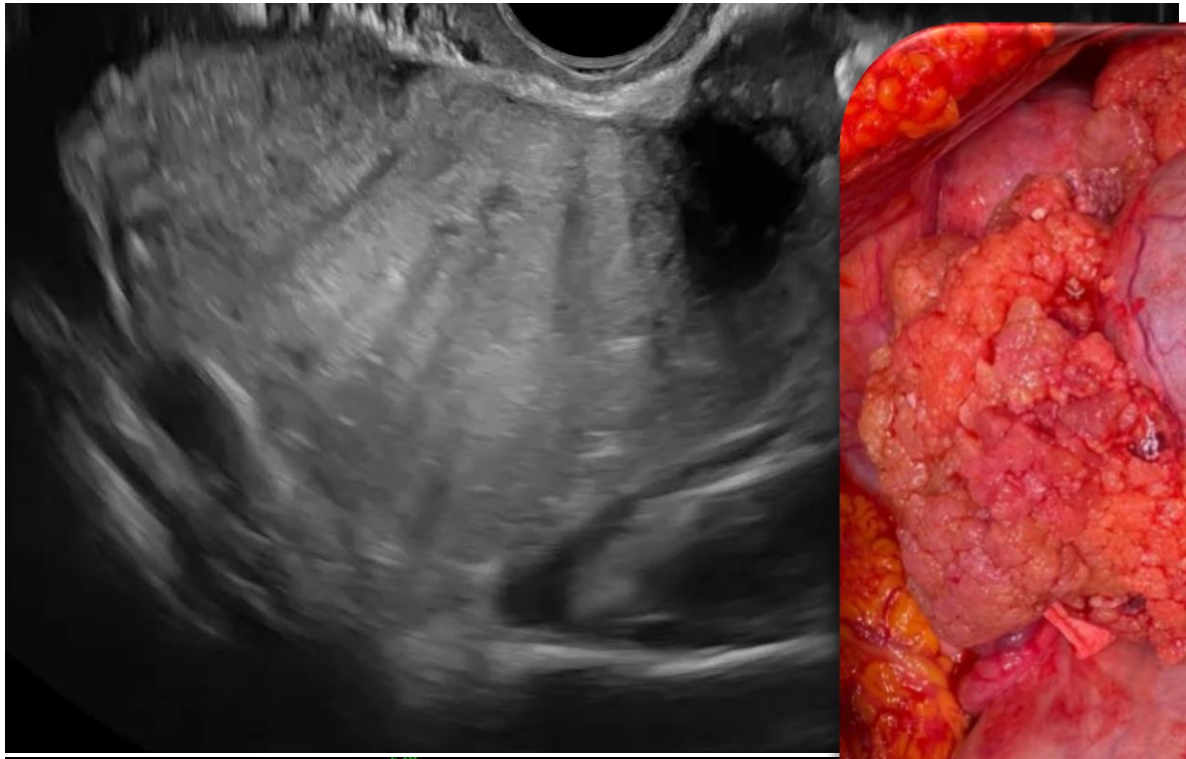
Serous BOT

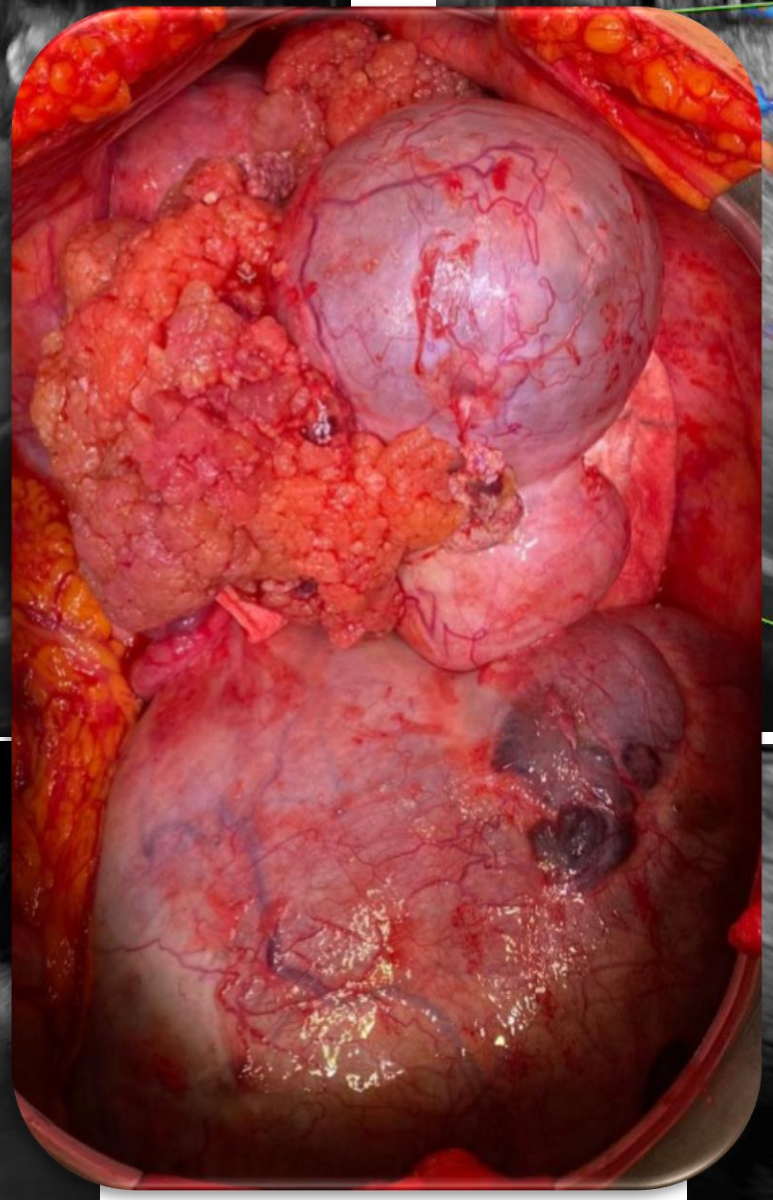


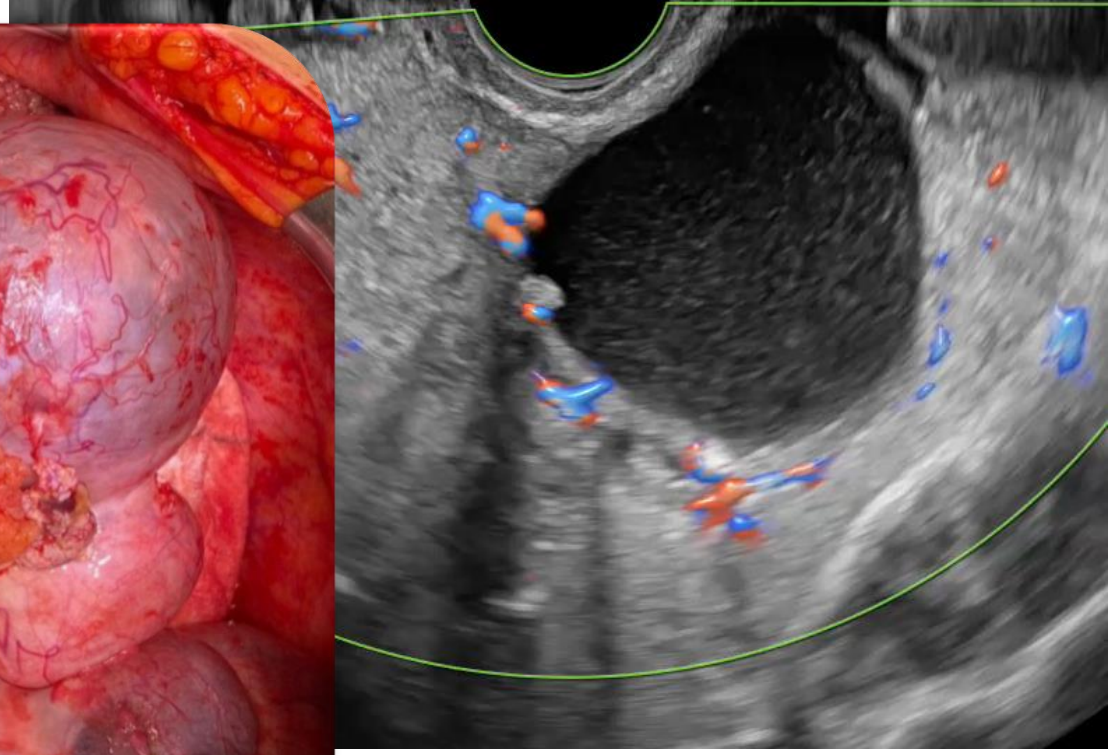
Solid Tumor

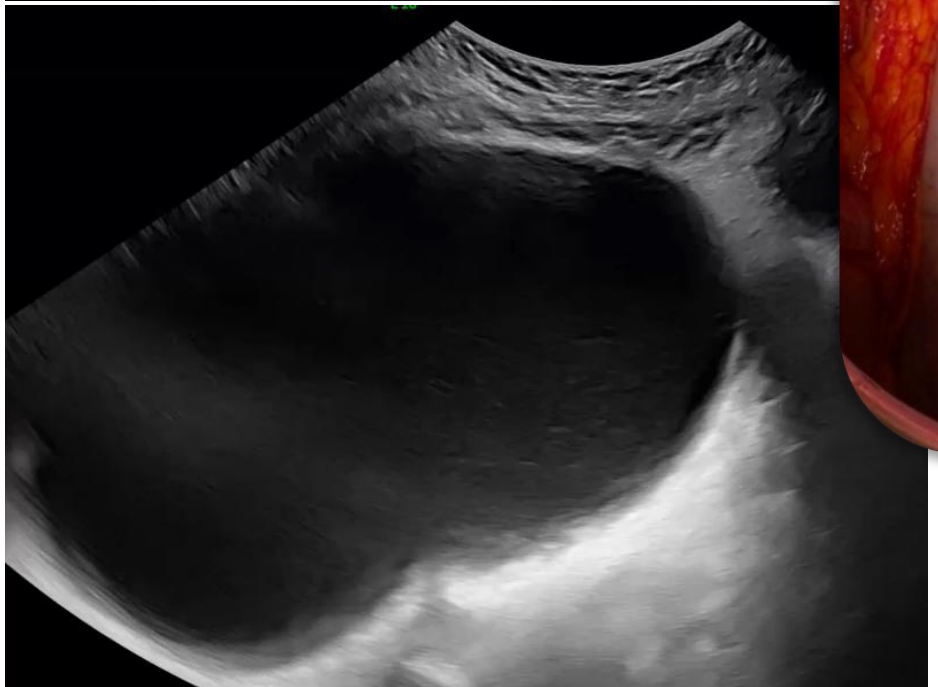


Serous BOT stage IA



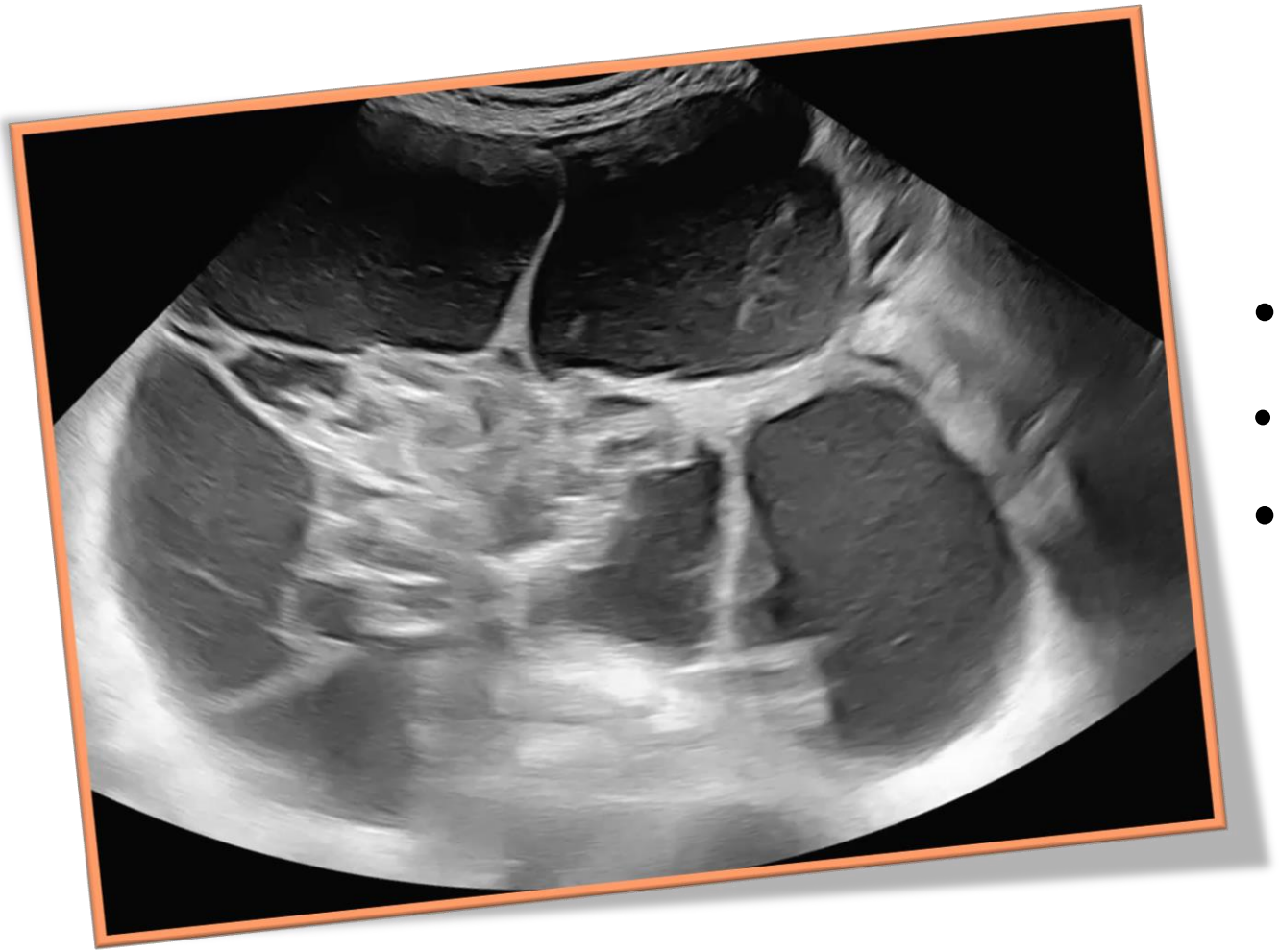






SEROUS BOT

Morphological features suggestive of intestinal type borderline tumor



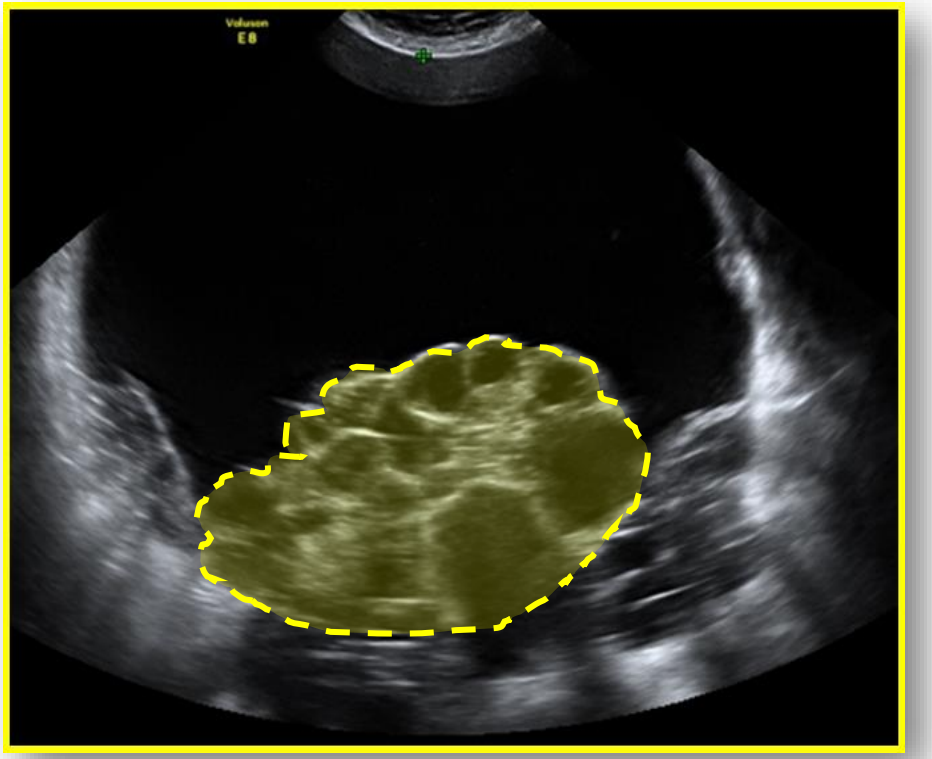
- Multilocular Cysts in 55% of cases
- > 10 locules in 80% of cases
- Thick echogenic fluid content

Yazbek UOG 2007

Ultrasound Obstet Gynecol 2007; 29: 489–495
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/uog.4002

Accuracy of ultrasound subjective 'pattern recognition' for the diagnosis of borderline ovarian tumors

J. YAZBEK*, K. S. RAJU†, J. BEN-NAGI*, T. HOLLAND*, K. HILLABY* and D. JURKOVIC*

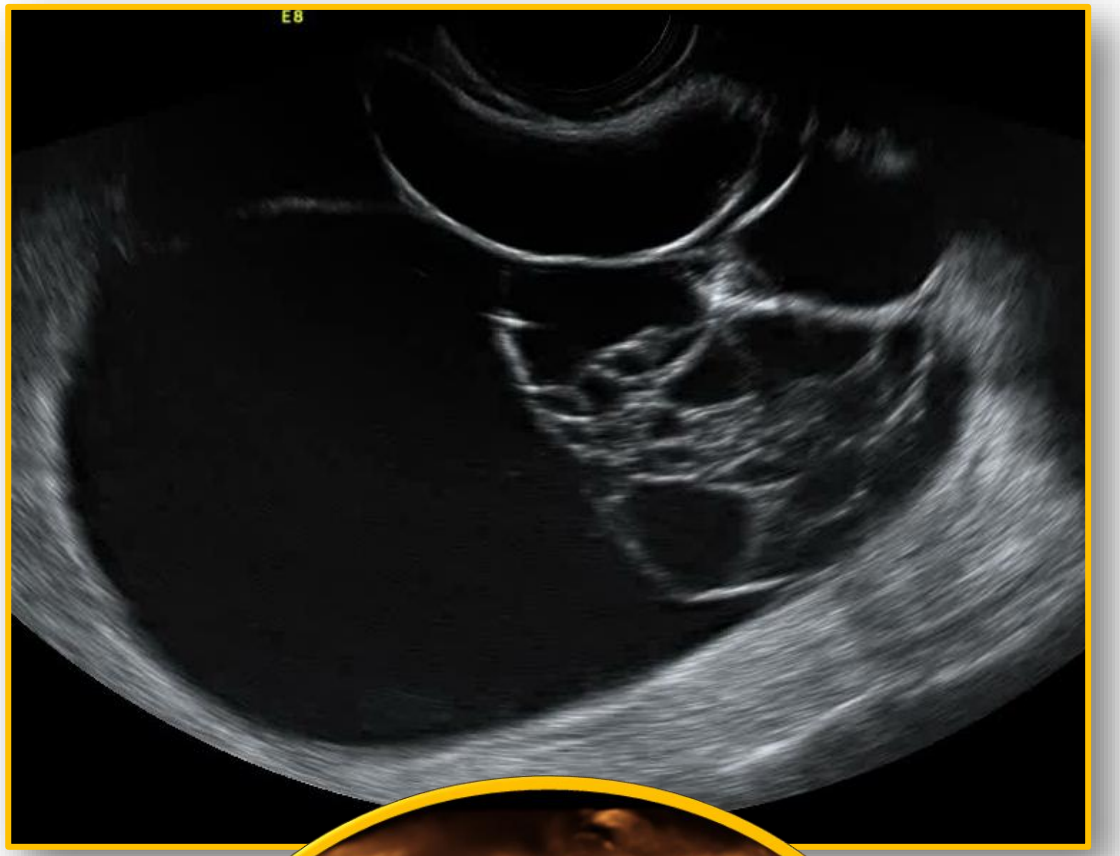


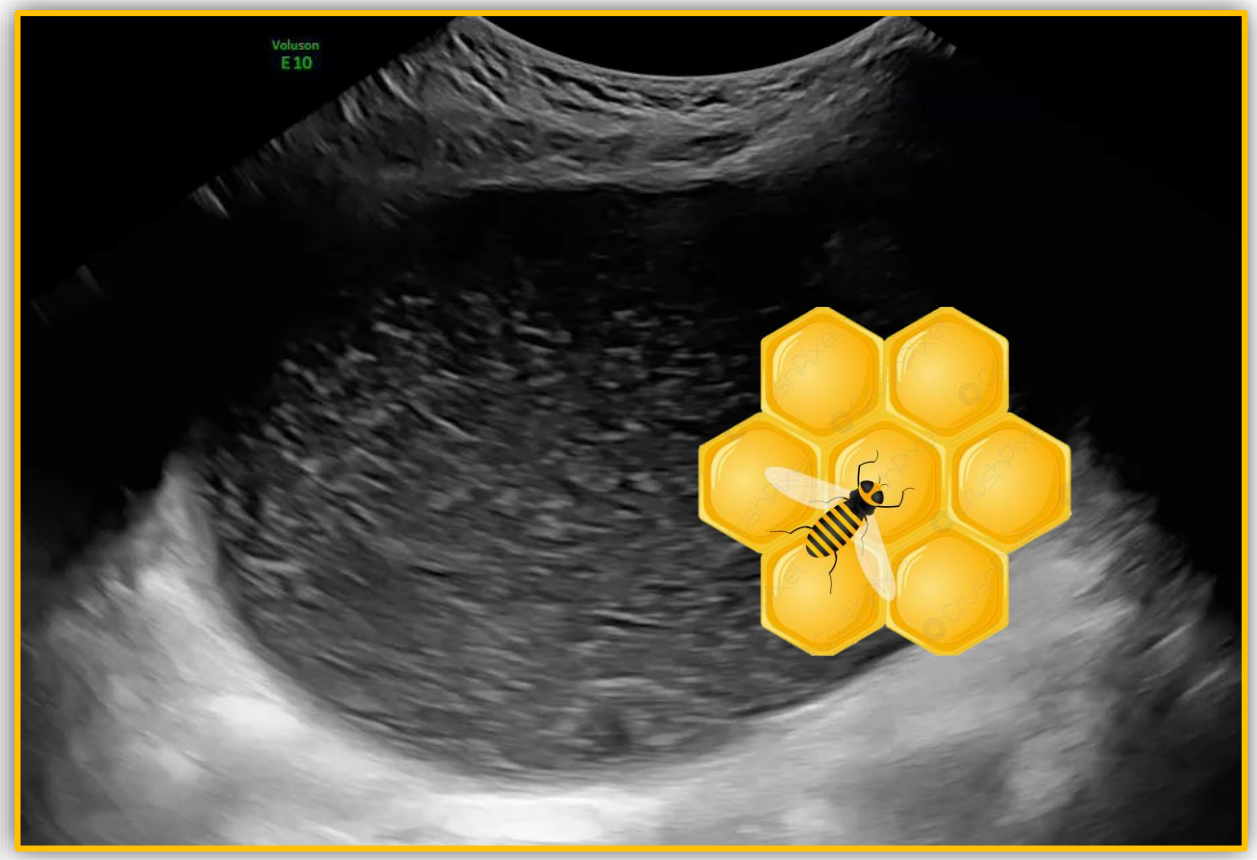
Honeycomb nodule

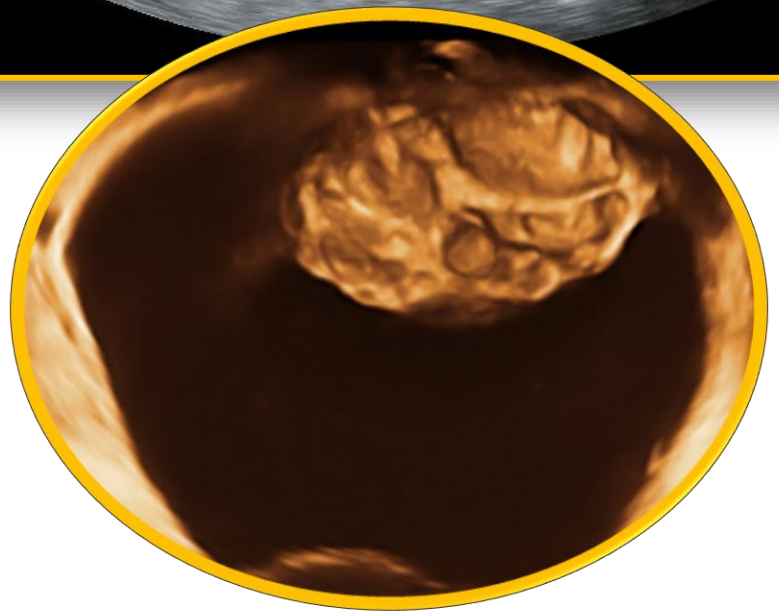
Specificity= 150/151 = 99%

Sensitivity= 8/15= 53%

A specific sign of intestinal type mucinous BOT







Borderline mucinous tumor Intestinal Type

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 30: 672–705, 2019
doi:10.1093/annonc/mdz062
Published online 2 May 2019

SPECIAL ARTICLE

ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease†

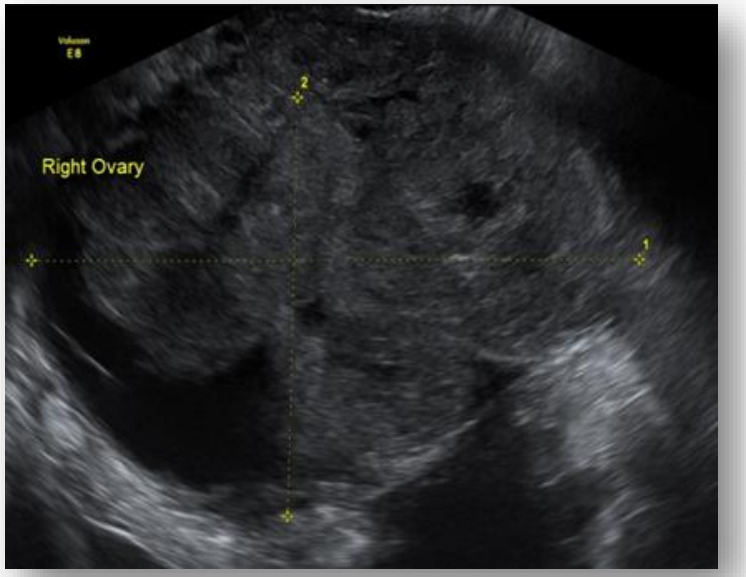
N. Colombo[1*], C. Sessa[2], A. du Bois[3], J. Ledermann[4], W. G. McCluggage[5], I. McNeish[6], P. Morice[7], S. Pignata[8], I. Ray-Coquard[9], I. Vergote[10,11], T. Baert[3], I. Belaroussi[7], A. Dashora[12], S. Olbrecht[10,11], F. Planchamp[13] & D. Querleu[14*], on behalf of the ESMO–ESGO Ovarian Cancer Consensus Conference Working Group‡

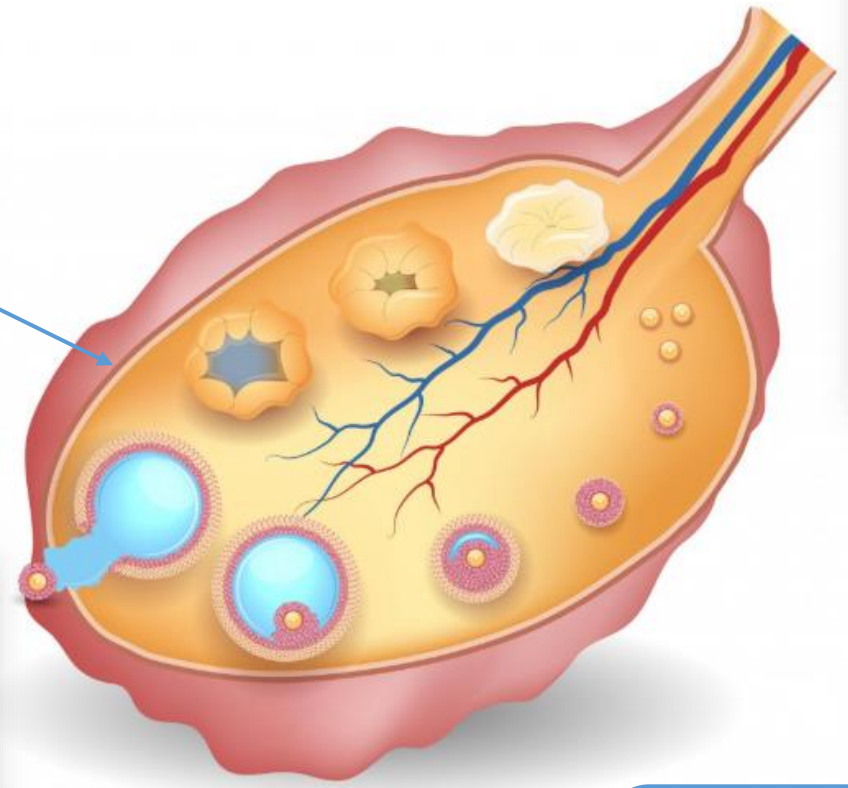
Recommendation 9.1: preservation of at least part of one ovary and the uterus is the standard approach in young patients with BOTs.
Level of evidence: III Strength of recommendation: A

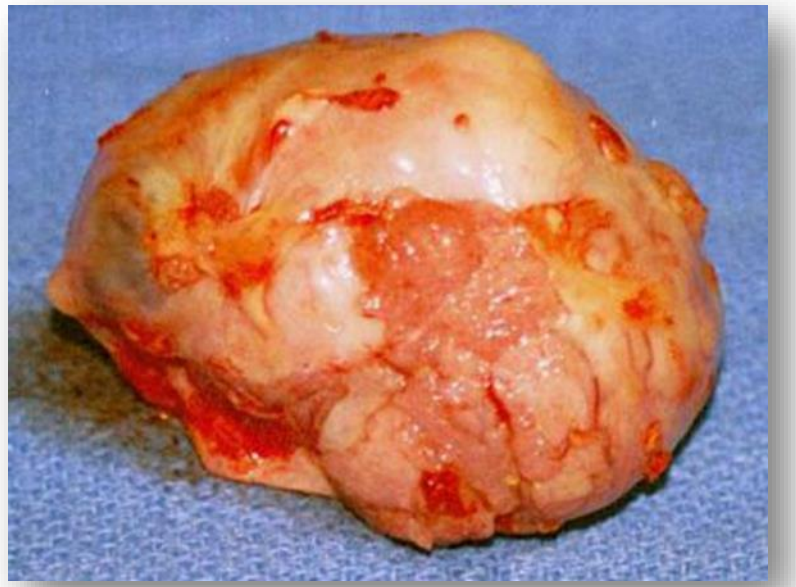
Recommendation 9.2: unilateral salpingo-oophorectomy is recommended with mBOTs to decrease the risk of invasive recurrence after cystectomy.
Level of evidence: IV Strength of recommendation: A

Recommendation 9.3: cystectomy is an acceptable management in sBOTs to preserve fertility.
Level of evidence: III Strength of recommendation: B

Epithelial
Ovarian tumors



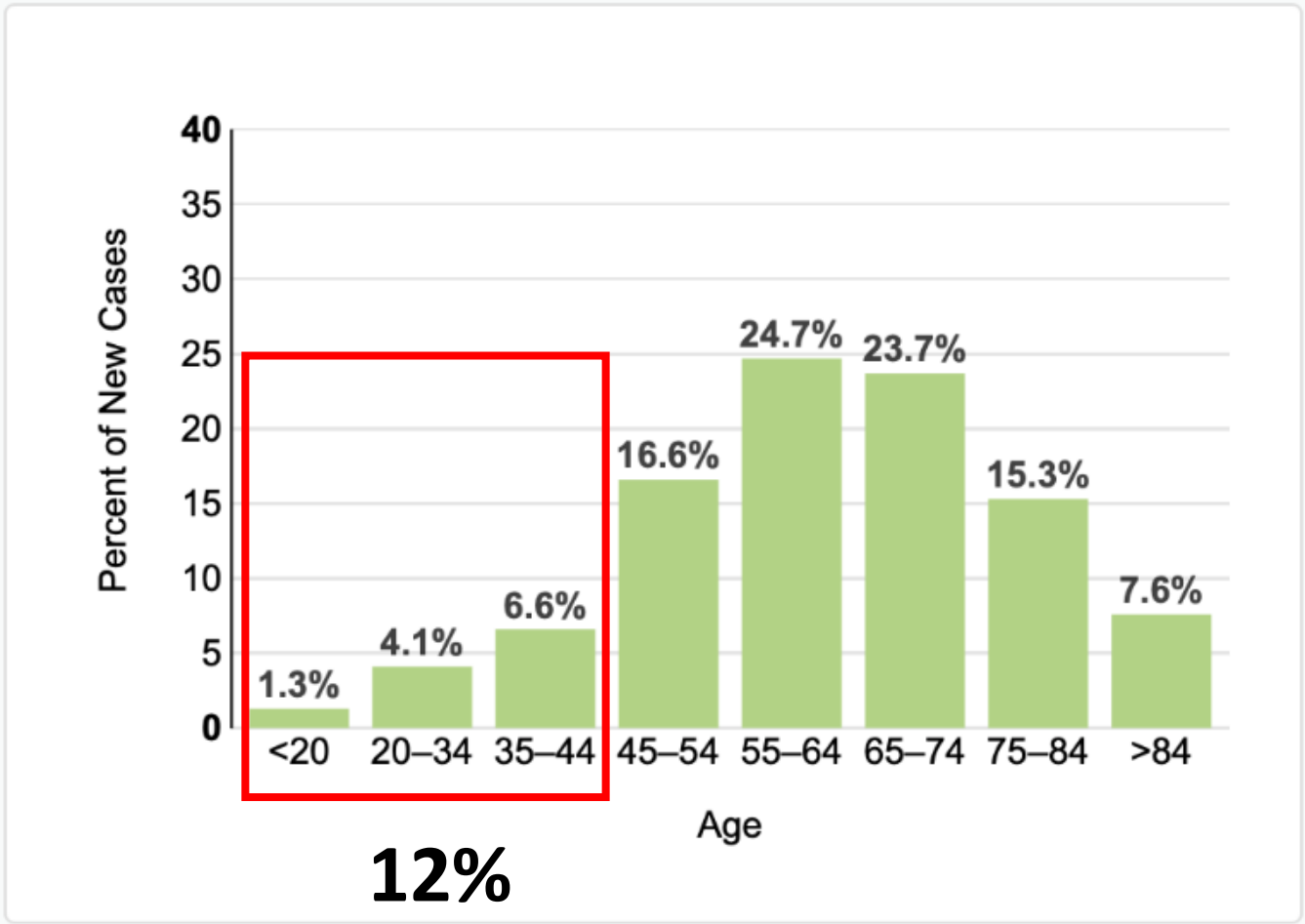




BOT Tumors

Primary Invasive tumors

Percent of New Cases by Age Group: Ovarian Cancer



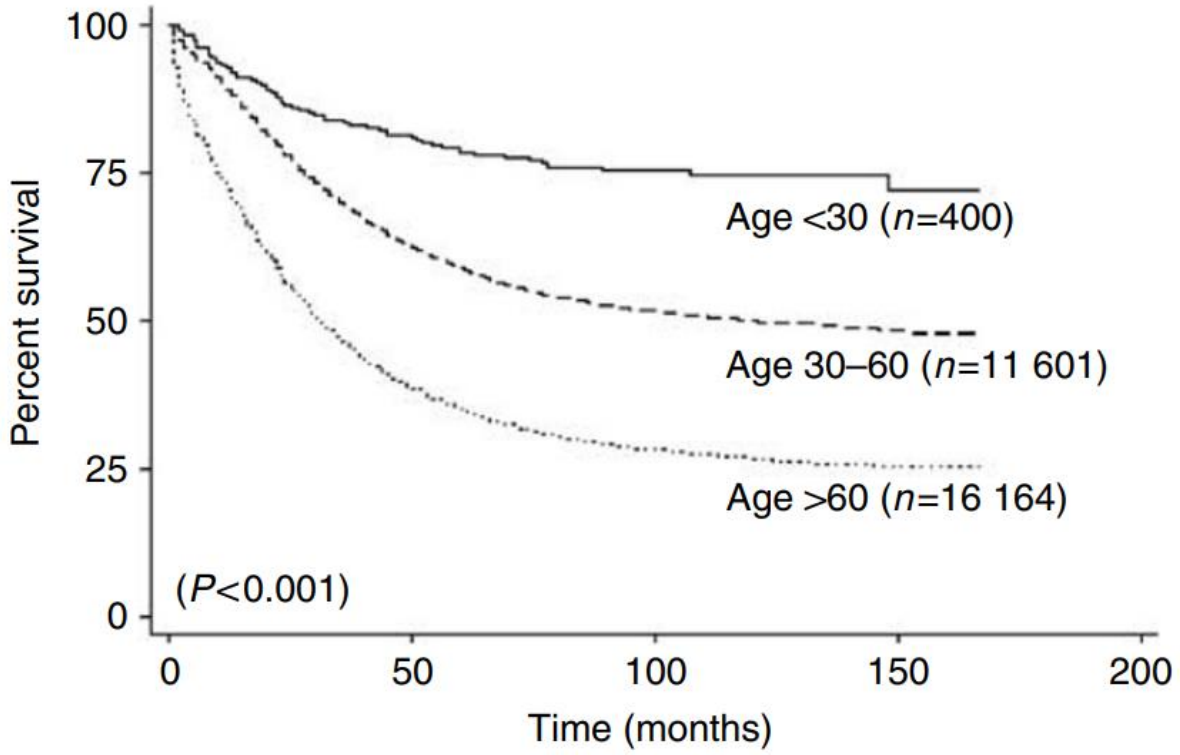
Ovarian cancer is most frequently diagnosed among women aged 55–64.

Median Age At Diagnosis

63

SEER 21 2014–2018, All Races, Females

Epithelial Ovarian Cancer in young patients



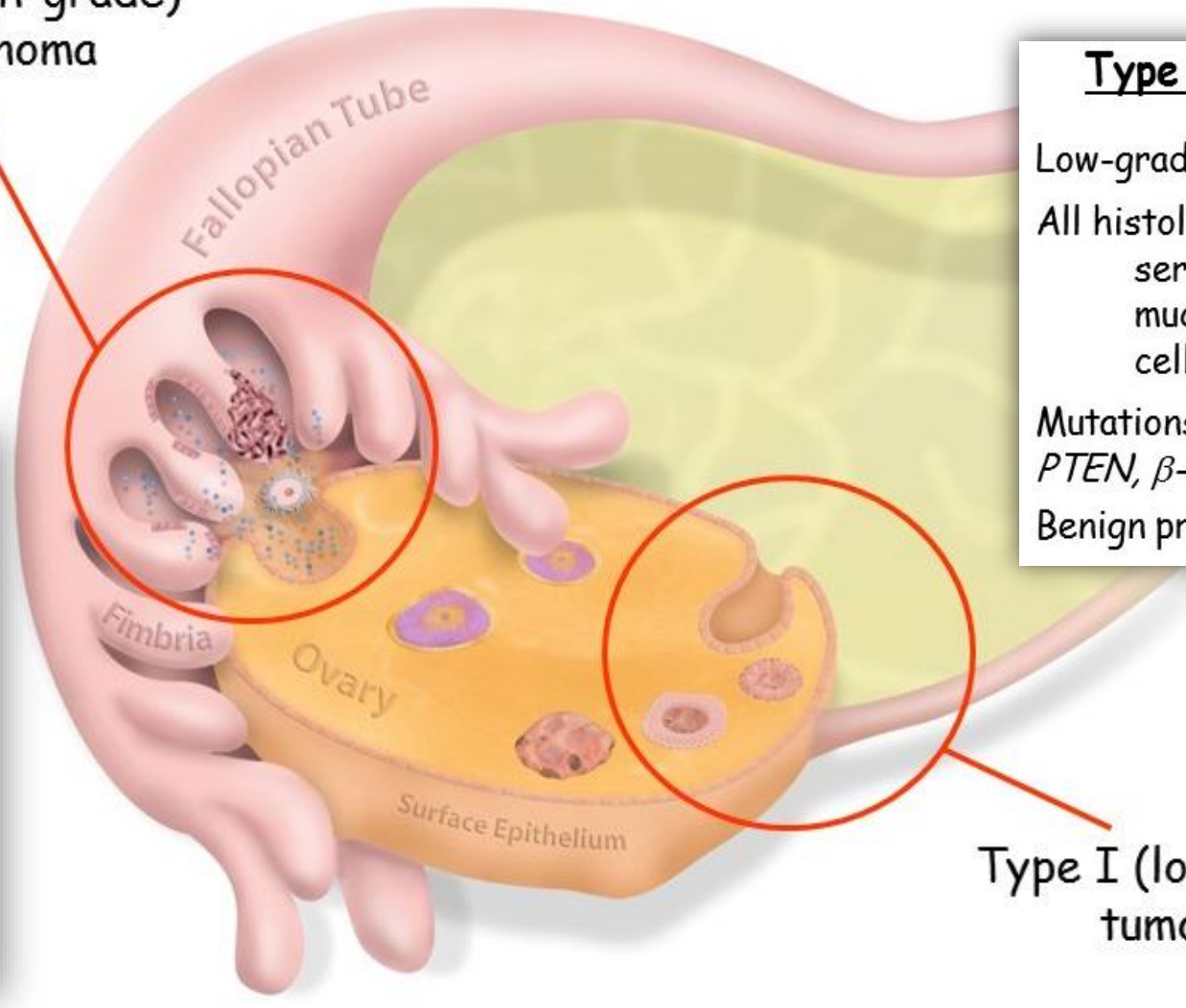
Disease specific survival of patients based on age at diagnosis

- More indolent grade 1 tumours
- Earlier stage
- Fertility Sparing surgery 70%

Chan JK. British Journal of Cancer 2006

Dualistic Model of OVCA Pathogenesis

Type II (high-grade) serous carcinoma



Type I (low grade) tumors

Type II tumors

High-grade, aggressive
Serous, endometrioid, carcinosarcoma, undifferentiated, and some clear cell carcinomas
Mutations in *TP53*
Mutations in *BRCA1*
No known ovarian precursor

Type I tumors

Low-grade, slow-growing
All histological subtypes, including serous (MPSC), endometrioid, mucinous, and some clear cell carcinomas
Mutations in *KRAS, BRAF, ERBB2, PTEN, β-catenin, ARID1A (BAF250)*
Benign precursors in ovary

Levanon et al, JCO 2008, Karst et al, JO 2010, Karst et al, F1000 2011; Jones et al, Frontiers Oncol 2013

Can we distinguish between the different subtypes of epithelial invasive ovarian cancer?

Determination of tumor-specific diagnosis

Ultrasound Obstet Gynecol 2017; 50: 788–799
Published online 2 November 2017 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.17414

Imaging in gynecological disease (12): clinical and ultrasound features of invasive and non-invasive malignant serous ovarian tumors

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Ultrasound Obstet Gynecol 2017; 50: 261–270
Published online 22 June 2017 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.17222

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F. MORO[1], G. F. ZANNONI[2], D. ARCIUOLO[2], T. PASCIUTO[1], S. AMOROSO[1], F. MASCILINI[1], S. MAINENTI[1], G. SCAMBIA[1] and A. C. TESTA[1]

Ultrasound Obstet Gynecol 2018; 52: 535–543
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.19026

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Ultrasound Obstet Gynecol 2018; 52: 792–800
Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/uog.19171

Imaging in gynecological disease (14): clinical and ultrasound characteristics of ovarian clear cell carcinoma

F. POZZATI[1], F. MORO[1], T. PASCIUTO[1], C. GALLO[2], F. CICCARONE[1], D. FRANCHI[3], R. MANCARI[3], S. GIUNCHI[4], D. TIMMERMAN[5,6], C. LANDOLFO[5,6], E. EPSTEIN[7], V. CHIAPPA[8], D. FISCHEROVA[9], R. FRUSCIO[10], G. F. ZANNONI[11], L. VALENTIN[12], G. SCAMBIA[1] and A. C. TESTA[2]

Low grade invasive Ovarian Cancer

Age	Laterality	Appearance	Typical features	CS
Median 53	Bilateral (60%)	Multilocular-solid (55%) Solid (32%)	Small Calcification in solid tissue (34%) Papillation (32%)	2/3/4

Ultrasound Obstet Gynecol 2017; **50**: 788–799
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ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumours

LGSOC Multilocular Solid: 55%
Hyperechoic foci 34%

Solid: 32%
Hyperechoic foci

Solid and hyperechoic

High grade invasive Ovarian Cancer

Age	Laterality	Appearance	Typical features	CS
55 - 65	Bilateral (60%)	Multilocular-solid (34%) Solid (64%)	Areas of necrosis in solid tissue Rarely papillation (7%)	2/3/4

Ultrasound Obstet Gynecol 2017; **50**: 788–799
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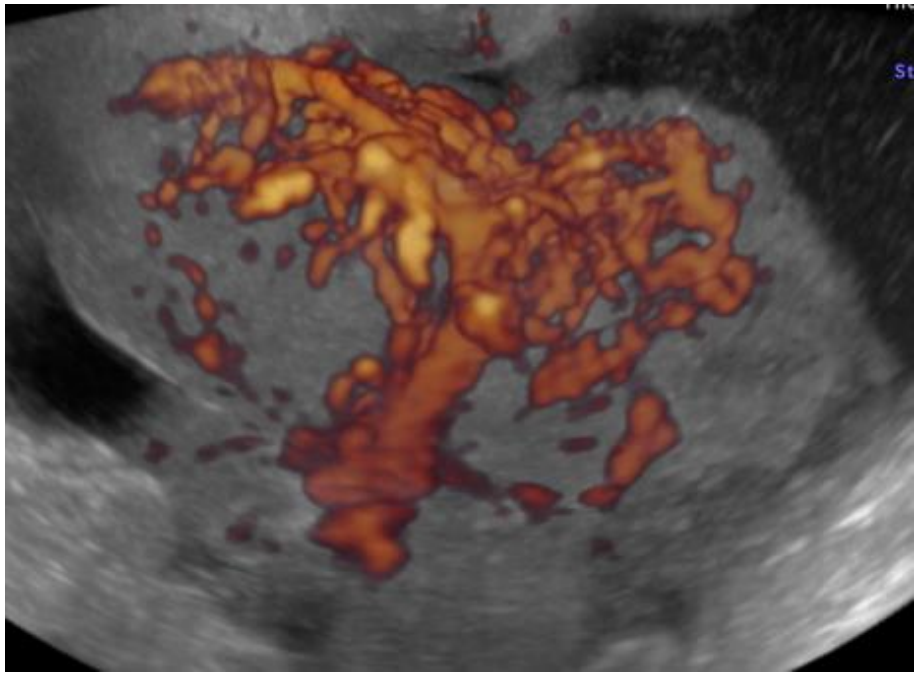
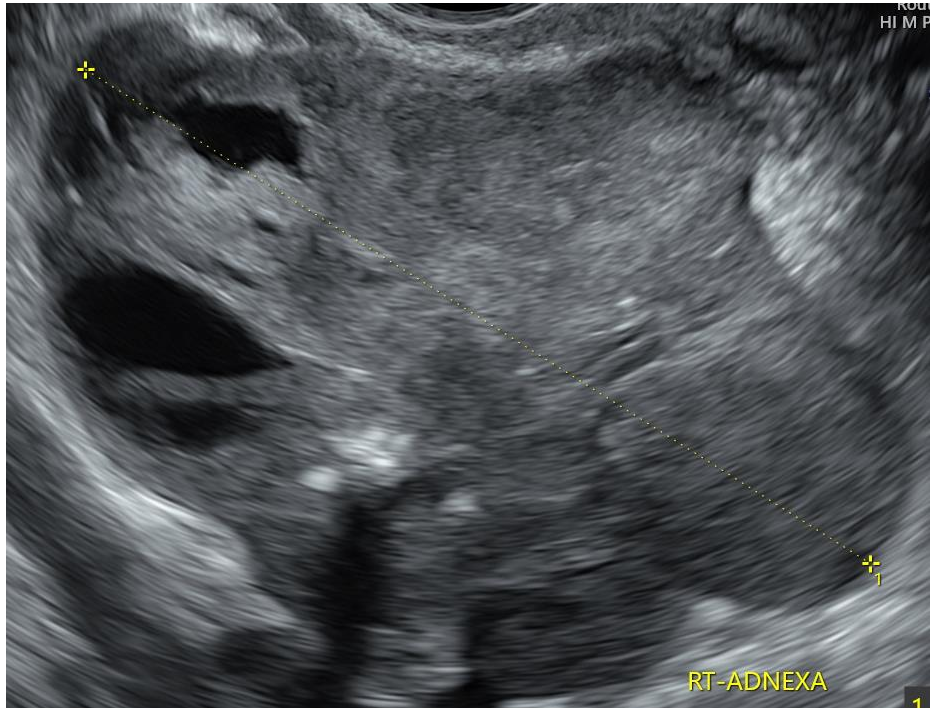
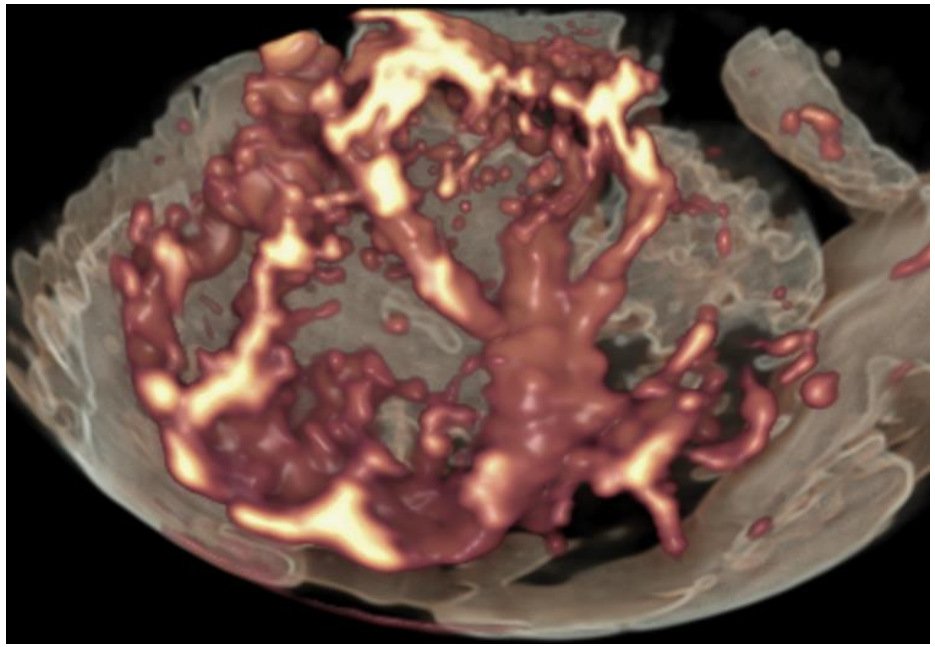
ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumours

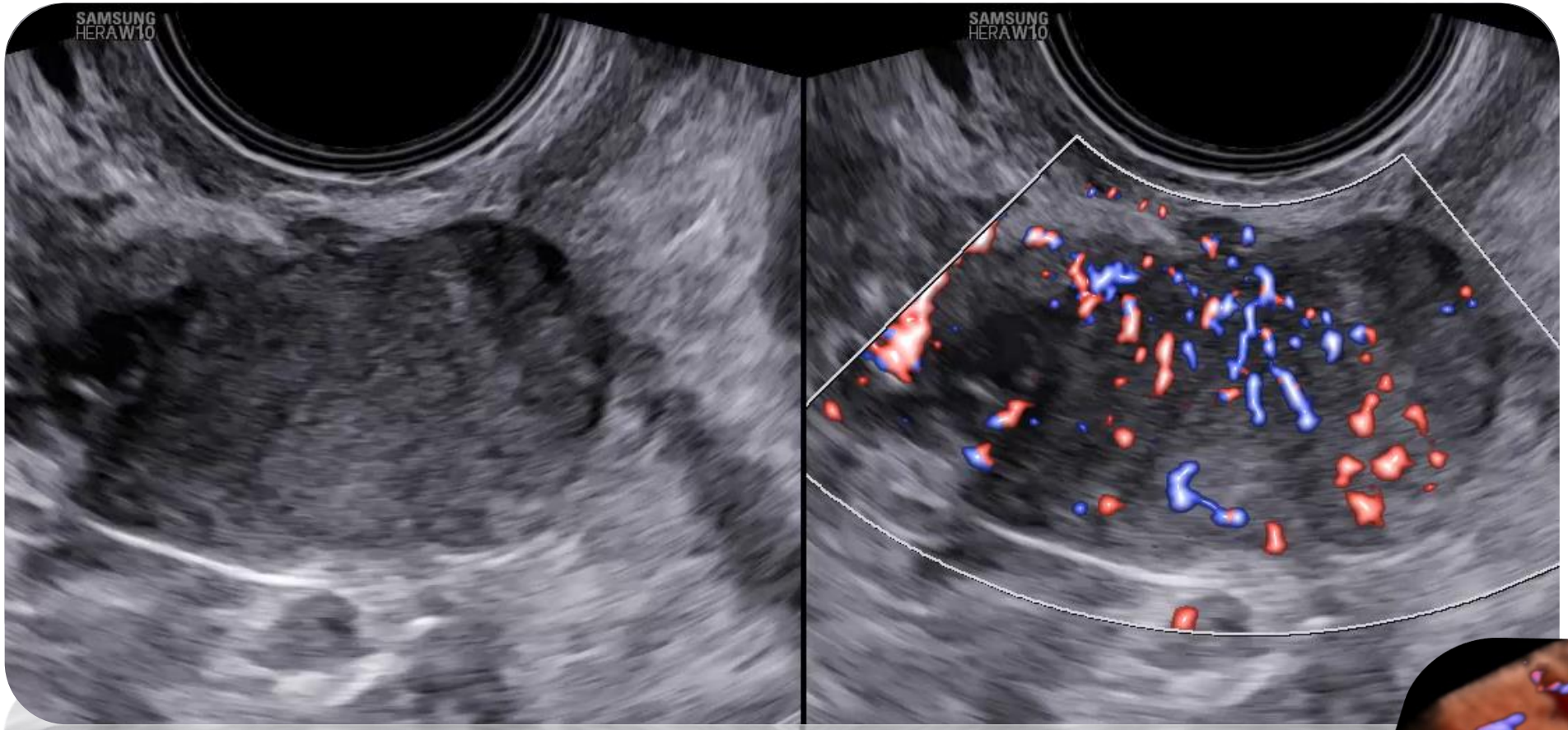
Multilocular Solid: 34%



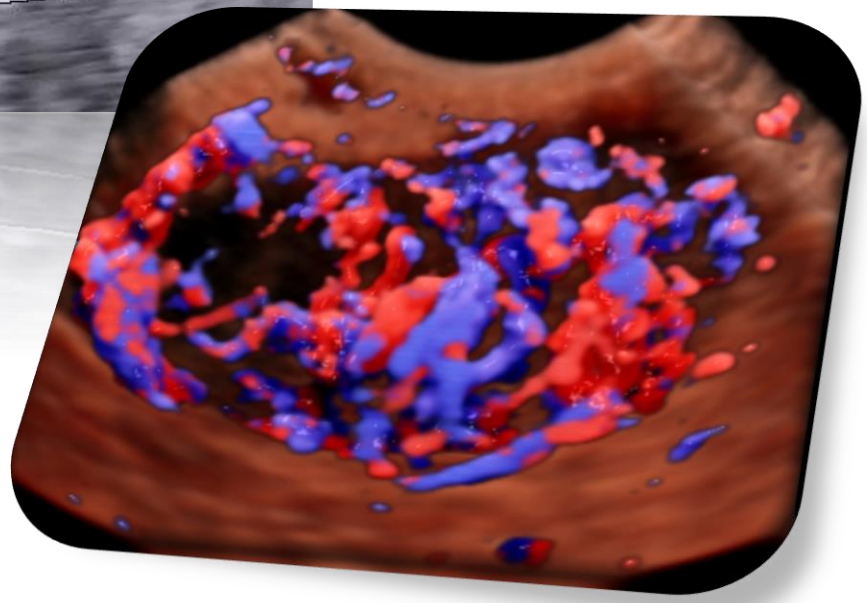




Solid: 64%



HGSOC
Stage IA G3



Endometrioid Ovarian Cancer

(10-15%)

Age	Laterality	Appearance	Typical features	CS
Median 55	Unilateral (79%) Coexist with endometrial carcinoma (20%)	Multilocular-solid (48%) With low-level (53%) or ground glass (16%) cystic fluid Solid (34%) Median diam 102 mm	Cockade-like appearance Papillations (29%) Develop from endometriosis (20%)	(2)/3/4

Imaging in gynecological disease (13): clinical and ultrasound characteristics of endometrioid ovarian cancer

F. MORO[1], G. MAGOGA[2], T. PASCIUTO[1], F. MASCILINI[1], M. C. MORUZZI[1], D. FISCHEROVA[3], L. SAVELLI[4], S. GIUNCHI[4], R. MANCARI[5], D. FRANCHI[5], A. CZEKIERDOWSKI[6], W. FROYMAN[7], D. VERRI[8], E. EPSTEIN[9], V. CHIAPPA[10], S. GUERRIERO[11], G. F. ZANNONI[12], D. TIMMERMAN[7], G. SCAMBIA[1], L. VALENTIN[13] and A. C. TESTA[2]

ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumours

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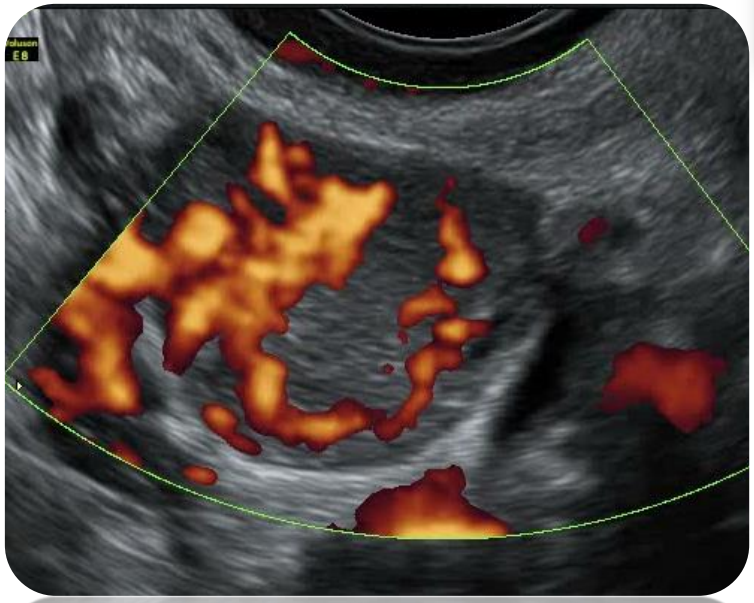
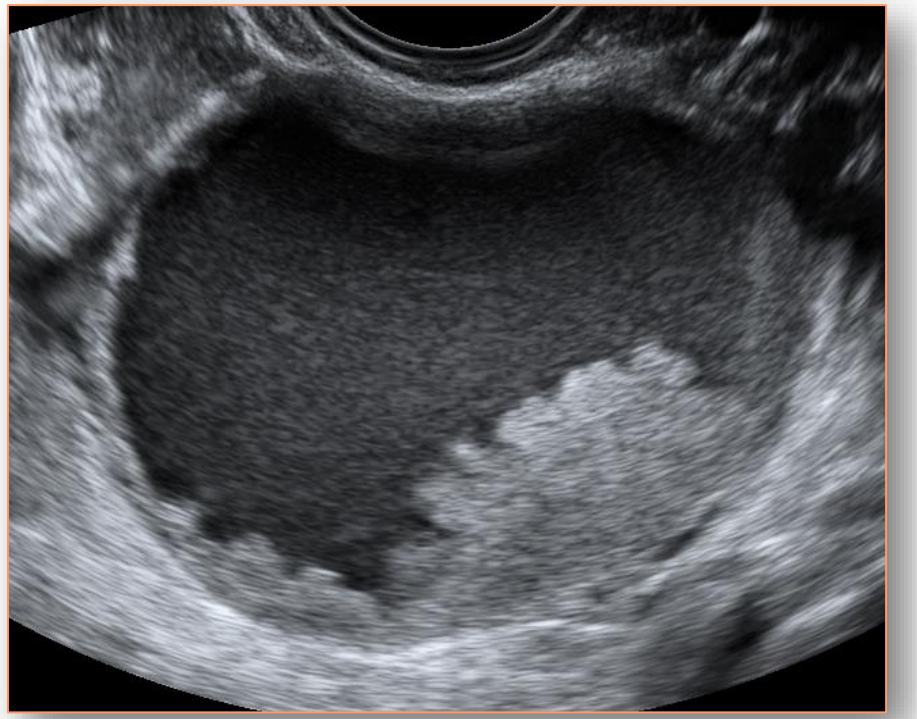
Tumor developing in Endometriosis

Unilateral
Papillary projection
Ground glass cystic fluid





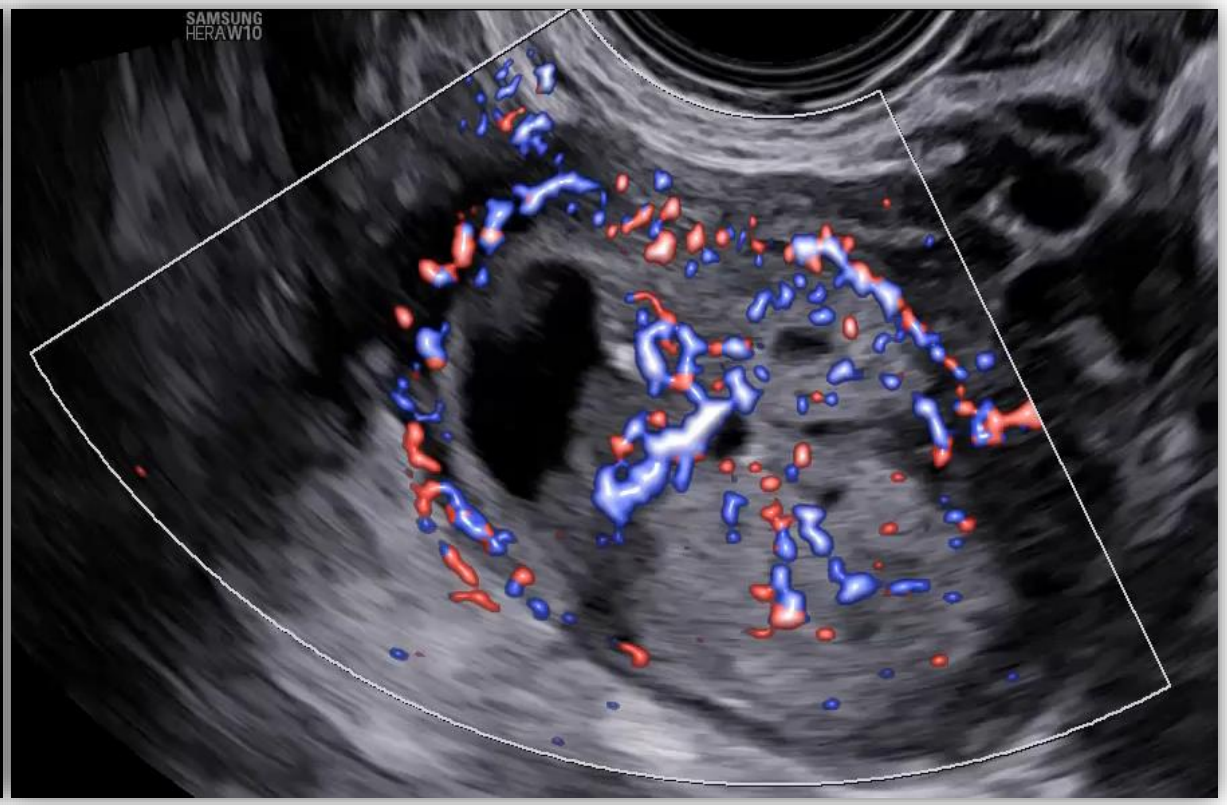
Unilocular Solid: 15,5%

Differential diagnosis BOT vs Invasive

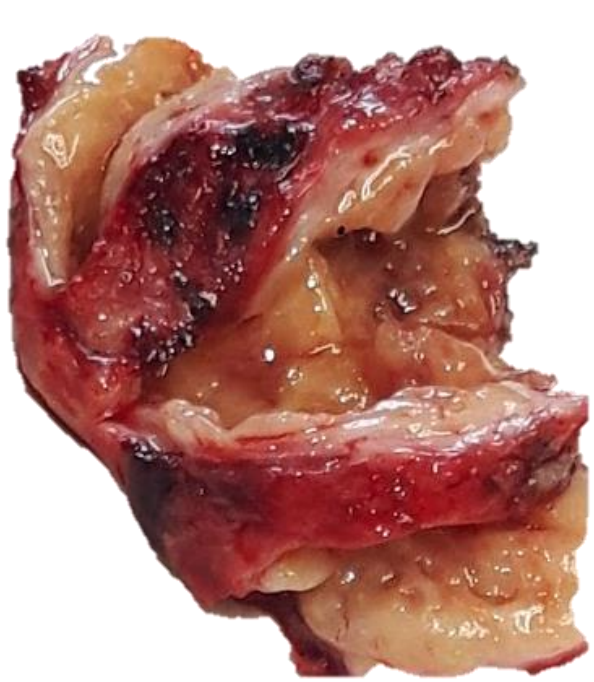
Serous BOT

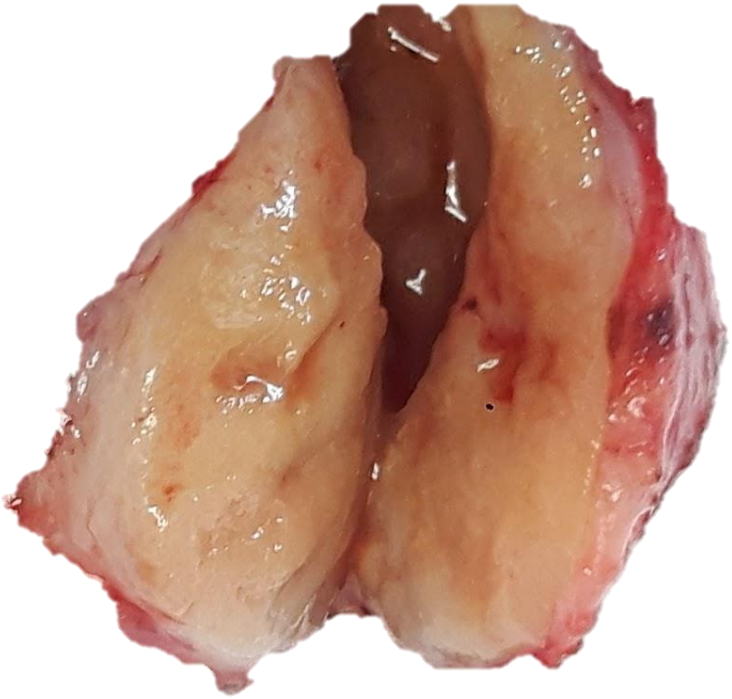
Endometrioid
Ov Cancer IA G1

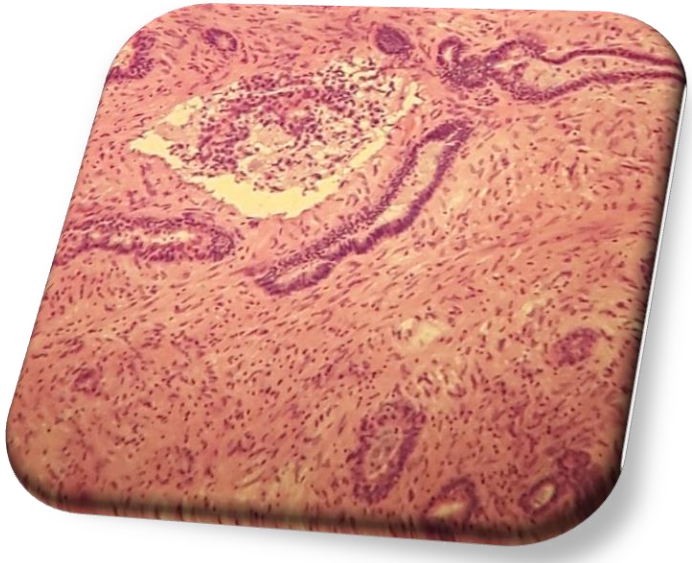
Non endometriosis related



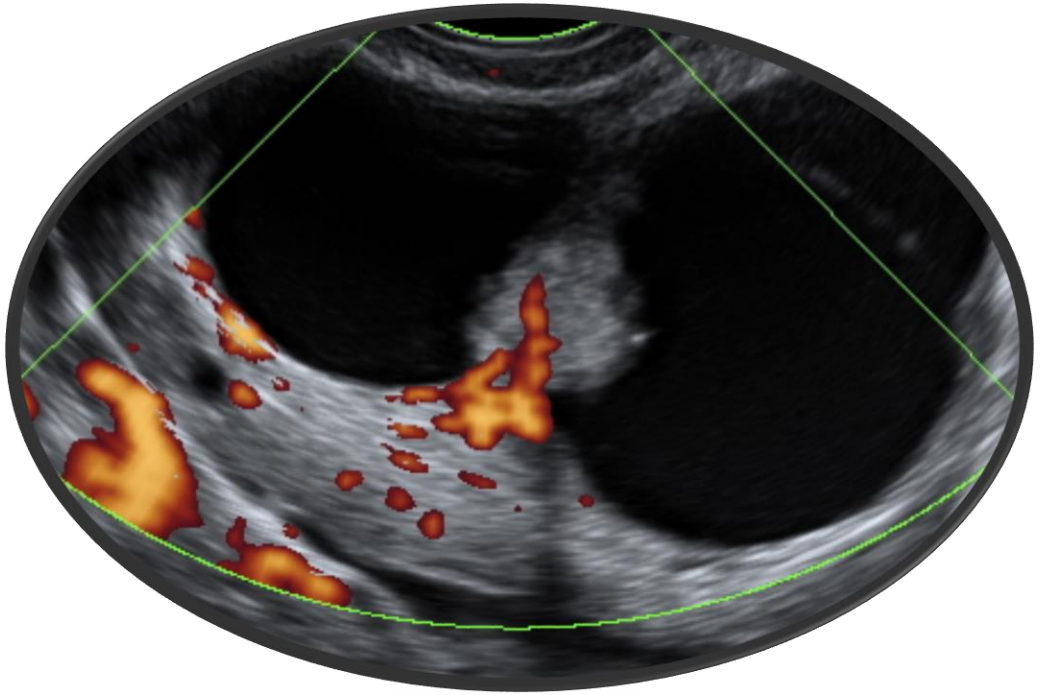
Multilocular Solid: 48%



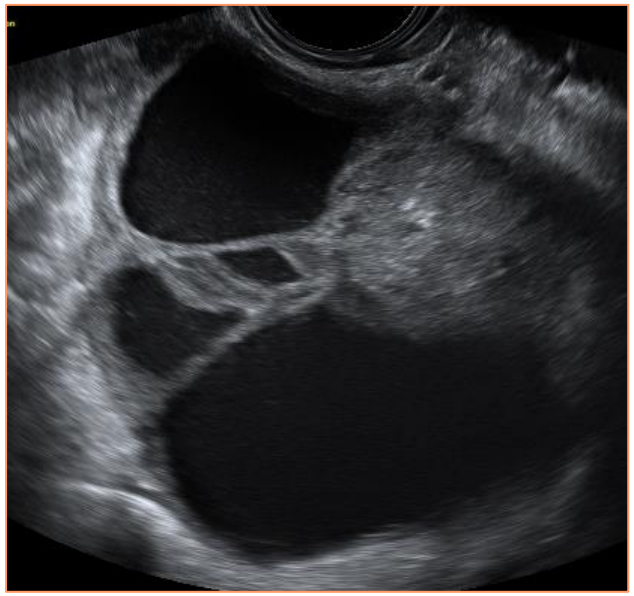


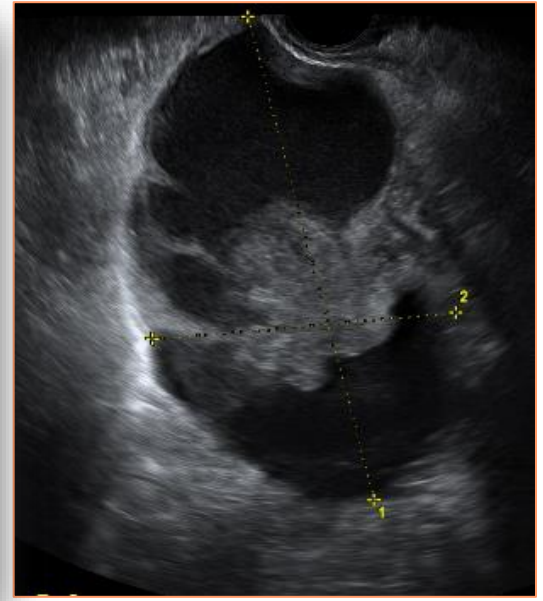


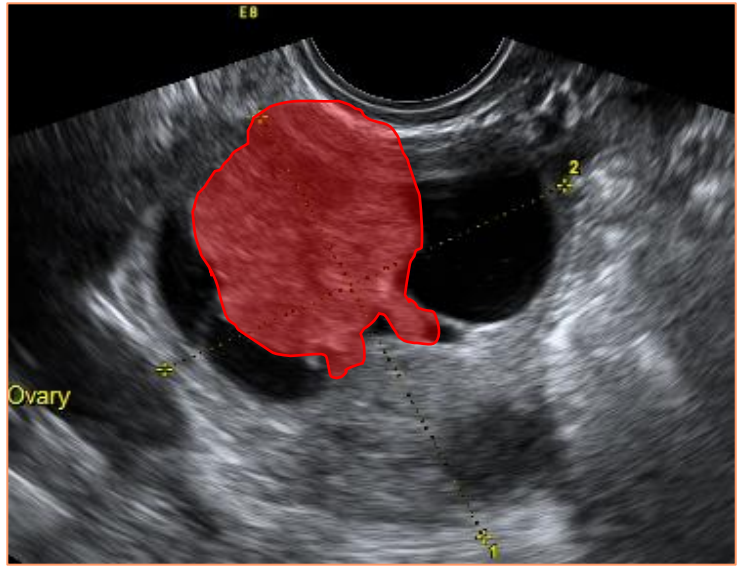
Endometrioid Ovarian Cancer Stage IA G1 and Endometrioid Borderline tumor

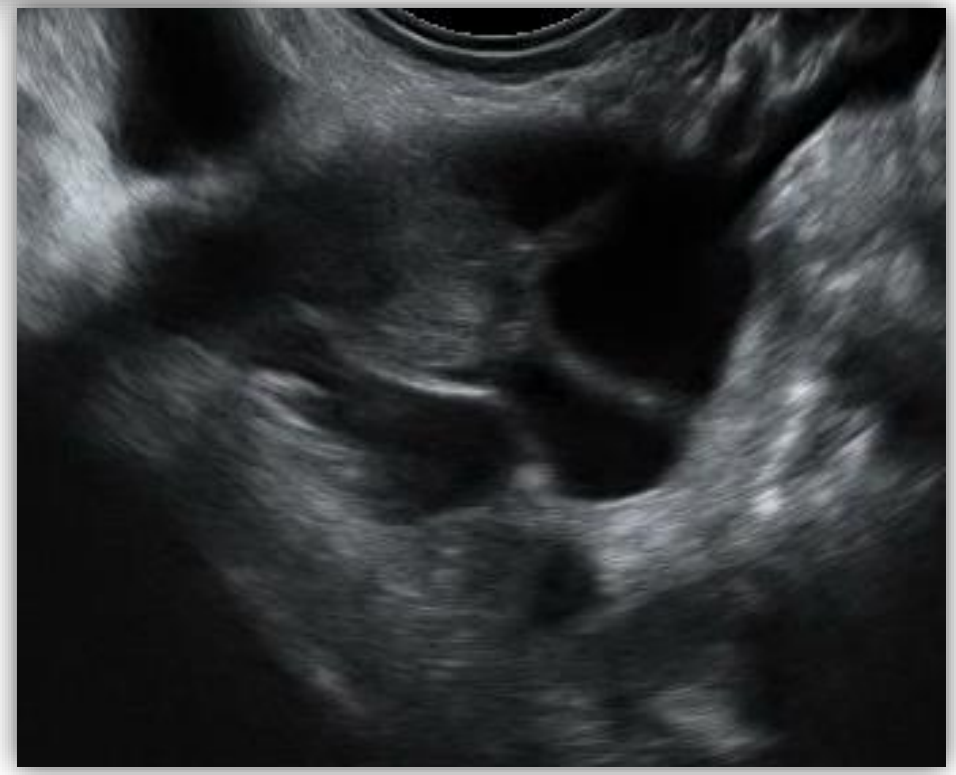


Endometrioid Ovarian Cancer
Stage IA G1









Cockade-like appearance

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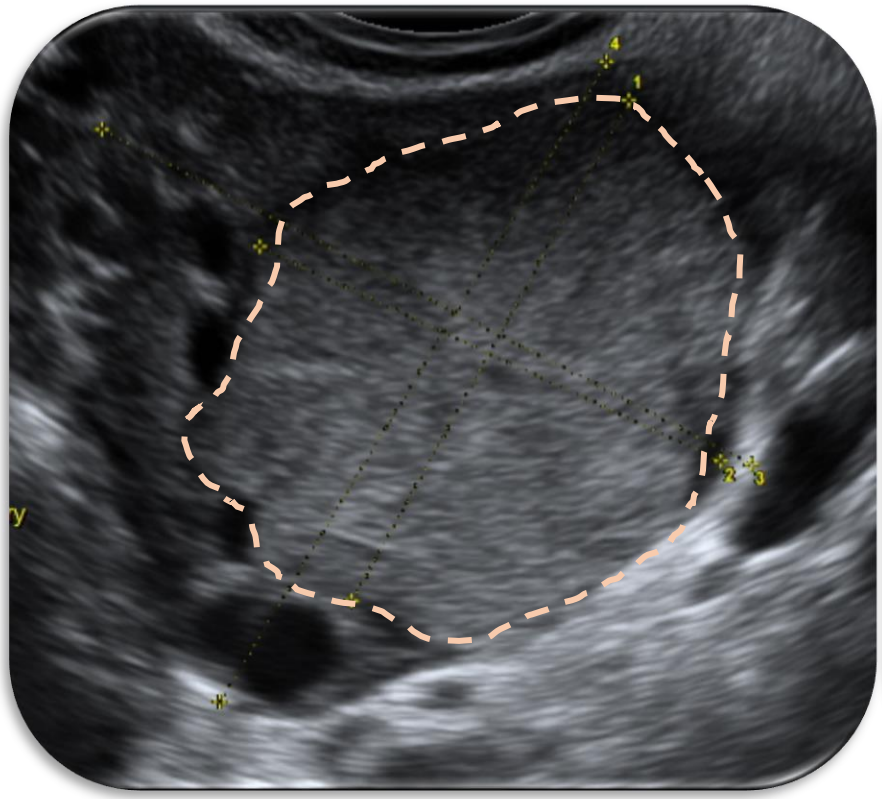
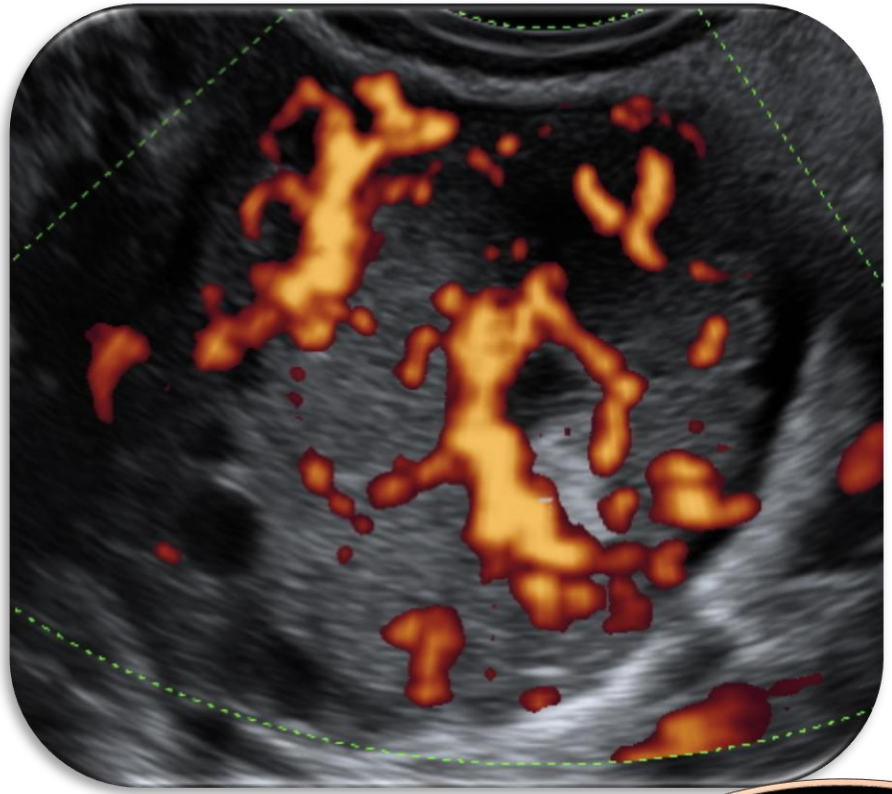
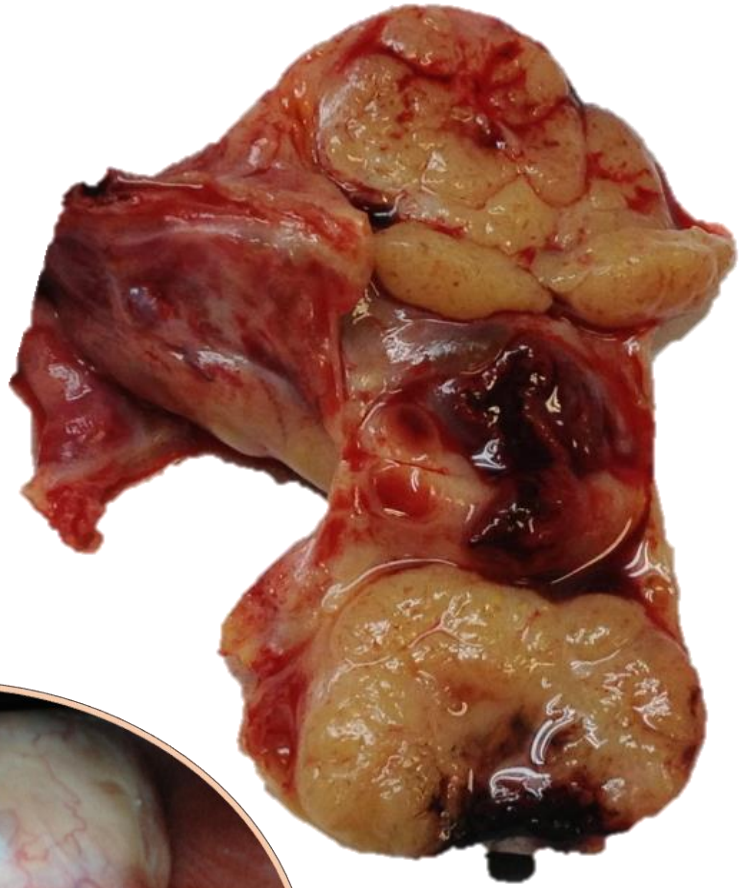
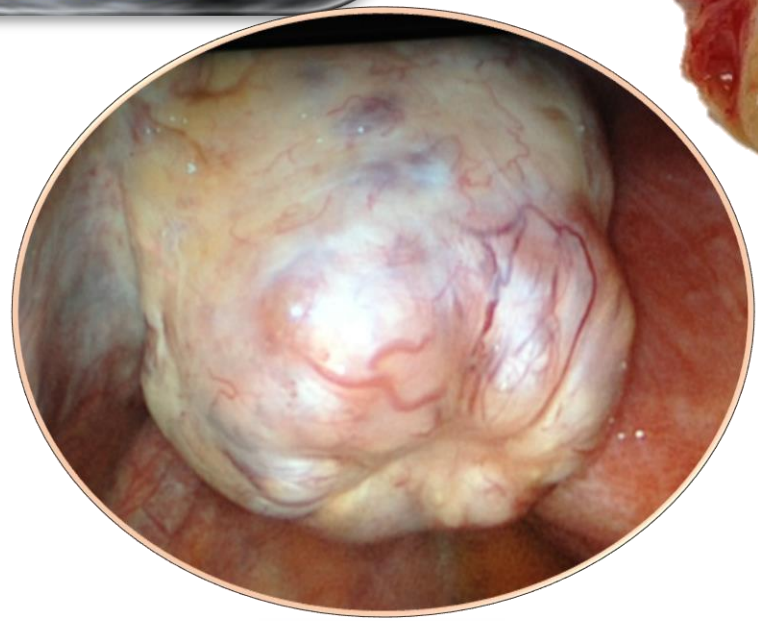
Solid with necrosis and haemorrage: 34%









Endometrioid Ovarian Cancer
Stage IA G1

Clear Cell Ovarian Cancer

(5-25%)

Age	Laterality	Appearance	Typical features	CS
Median 55	Unilateral (85%)	Multilocular-solid (41%) Unilocular solid (35%) with low-level (44%) or ground glass (22%) cystic fluid Solid (24%) Median diam 117 mm	Solid Nodules Papillations (38%) Develop from endometriosis (20-30%)	(2)/3/4

Imaging in gynecological disease (14): clinical and ultrasound characteristics of ovarian clear cell carcinoma

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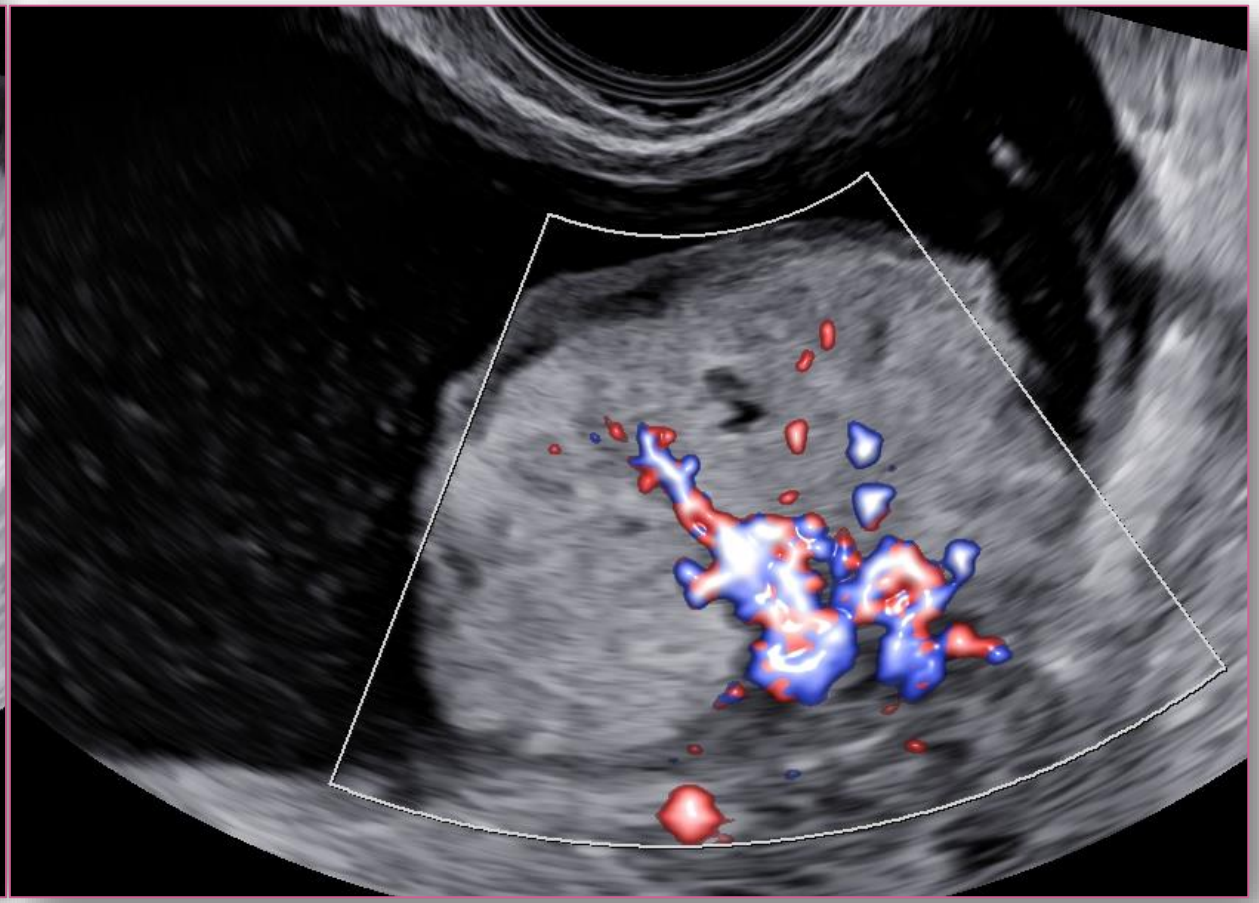
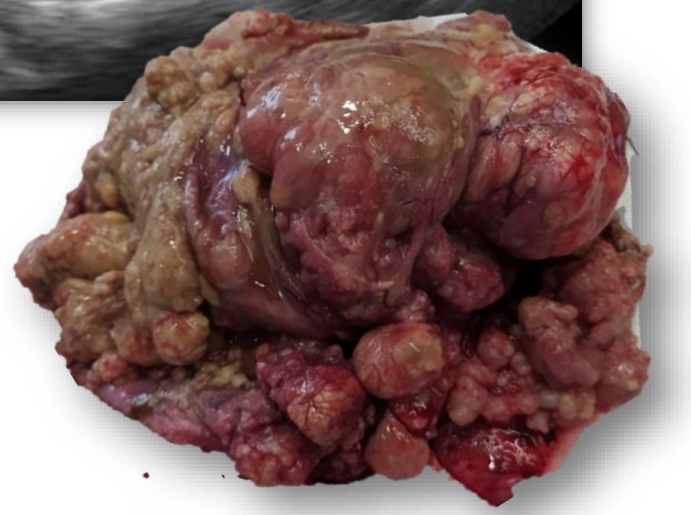
ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumours

Unilocular Solid: 35%

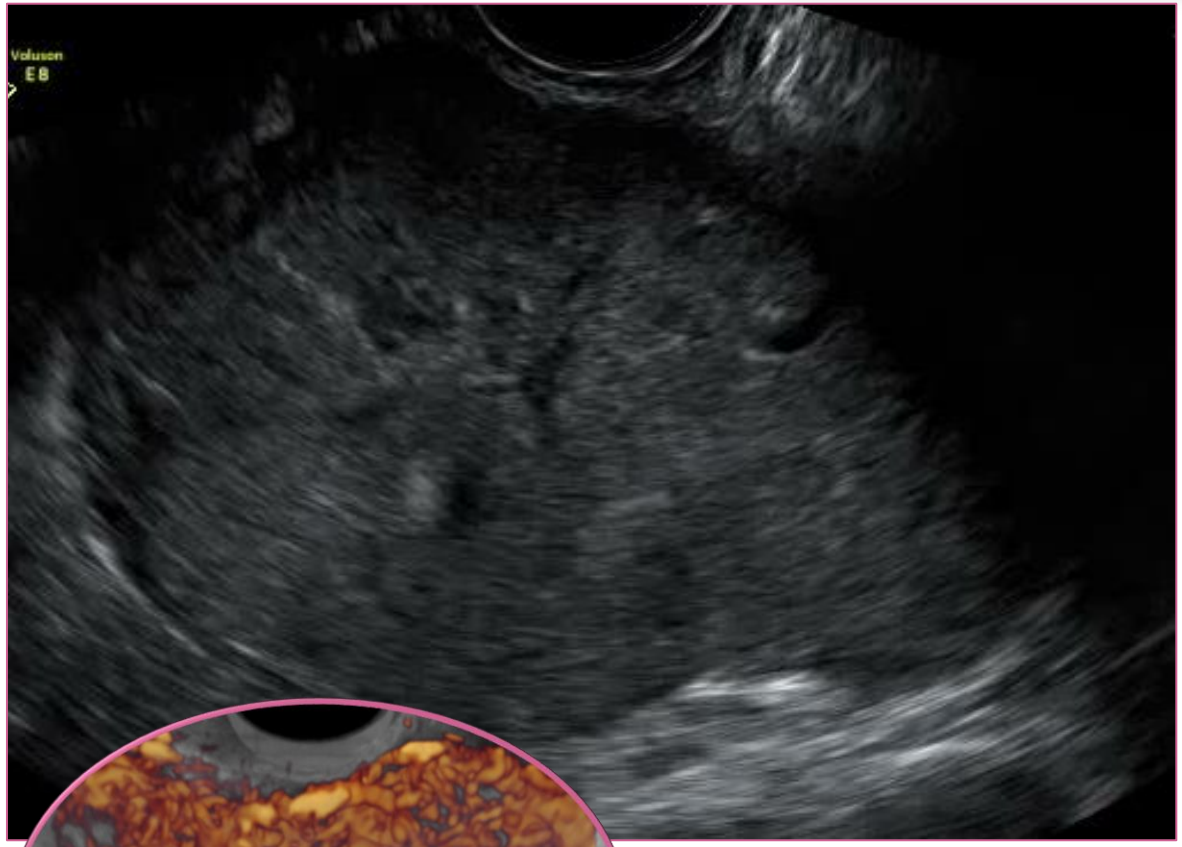


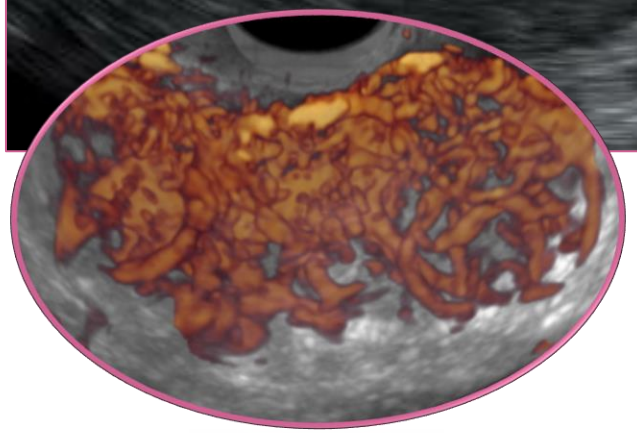
Multilocular Solid: 41%

Thick walled unilocular-solid cysts with multiple yellow-beige fleshy nodules protruding into the lumen



Solid: 24%





Mucinous Ovarian Cancer

(3%)

Age	Laterality	Appearance	Typical features	CS
Median 53	Unilateral (80%)	Multilocular-solid (55%) Multilocular or Solid	Very large tumor (median diameter 197 mm) > 10 locules 67% Cystic fluid low level (73%)	2/3/(4)

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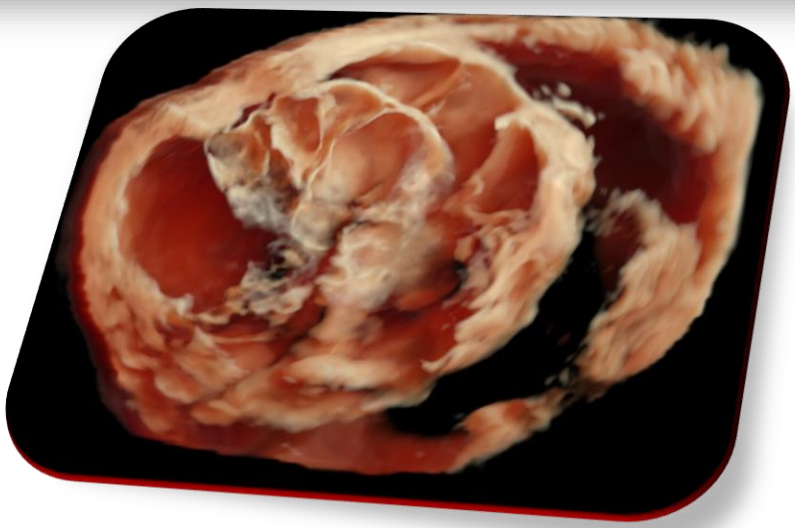
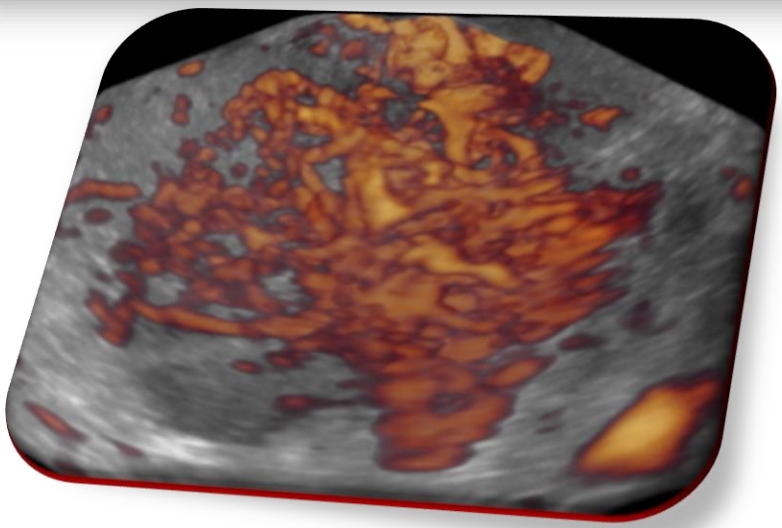
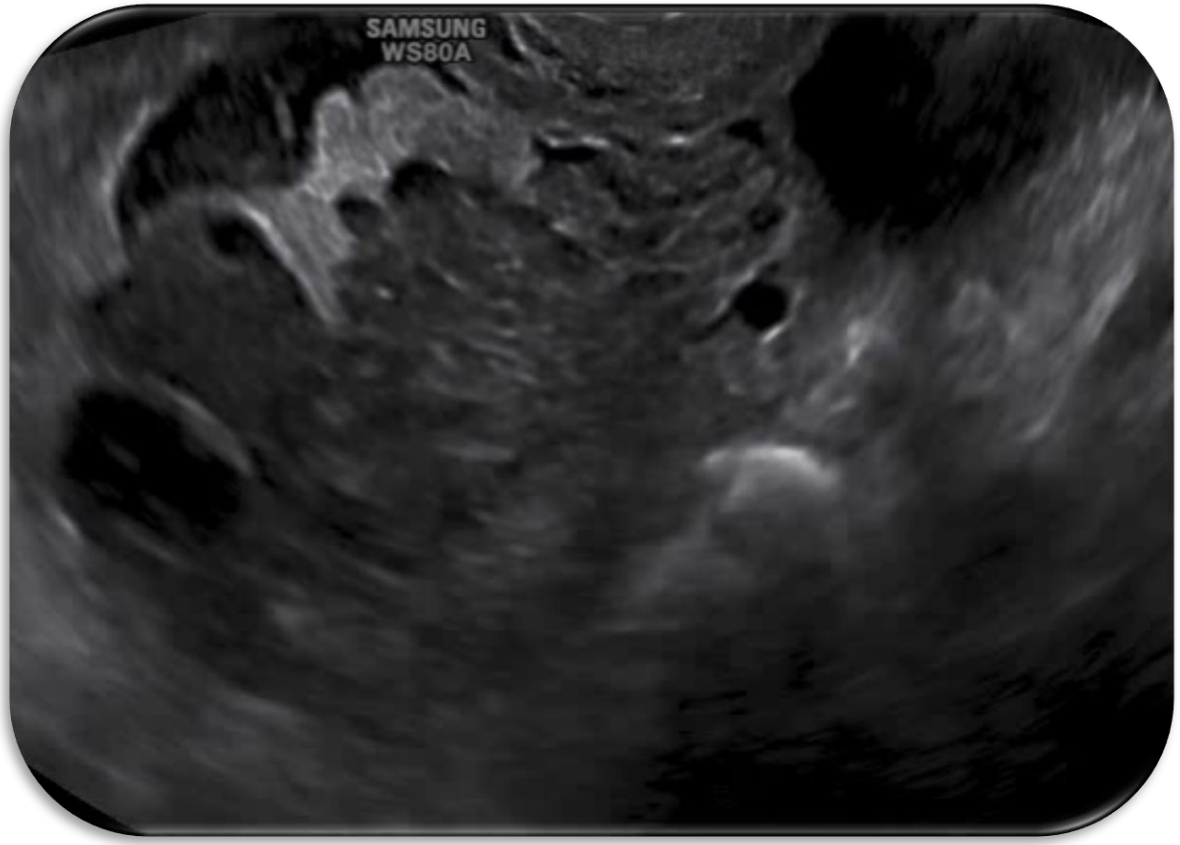
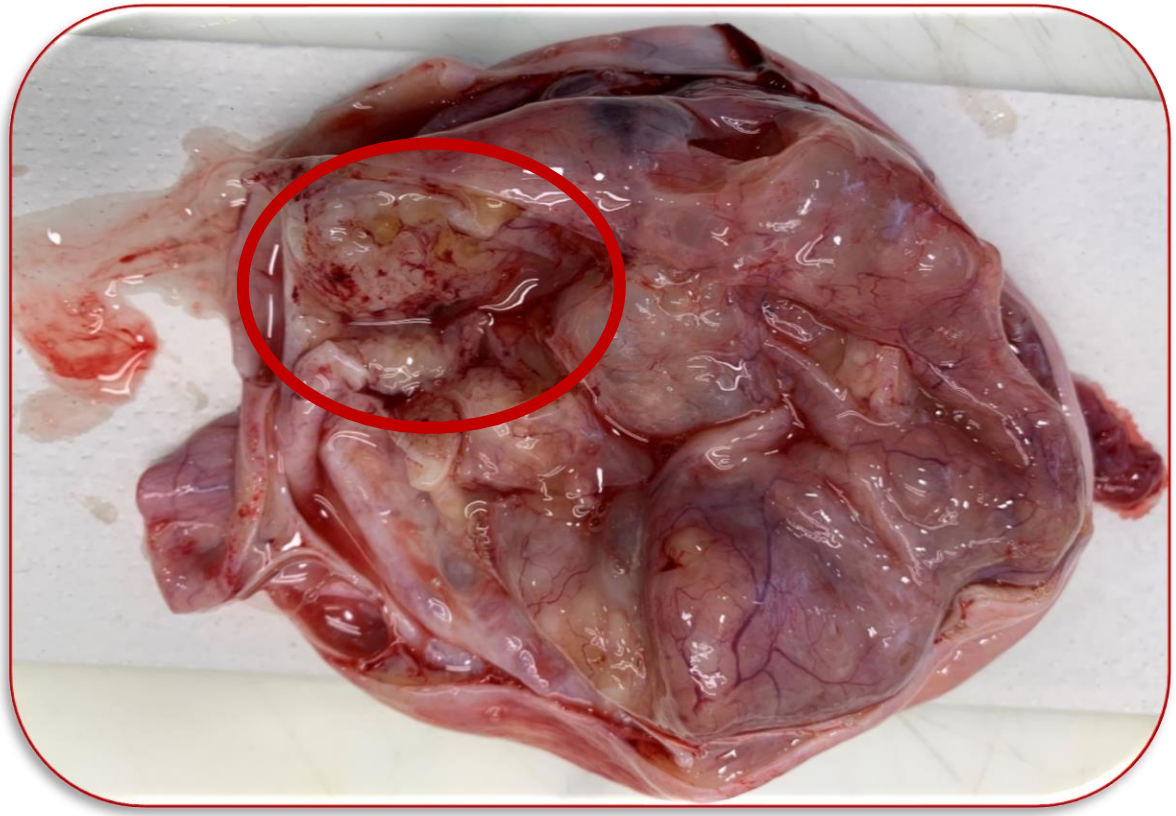
F. MORO[1], G. F. ZANNONI[2], D. ARCIUOLO[2], T. PASCIUTO[1], S. AMOROSO[1], F. MASCILINI[1], S. MAINENTI[1], G. SCAMBIA[1] and A. C. TESTA[1]

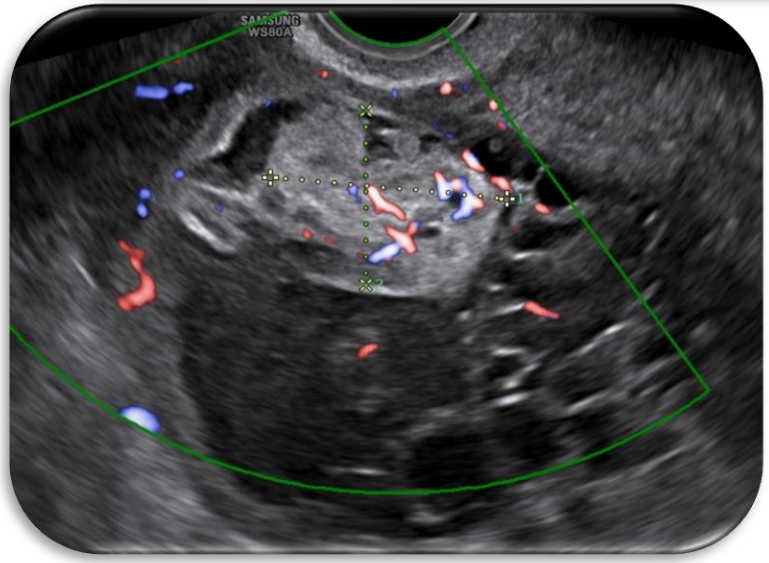
ESGO/ISUOG/IOTA/ESGE Consensus Statement on preoperative diagnosis of ovarian tumours











Mucinous adenocarcinoma
(expansile growth)
with focal microinvasion
in prevalent Mucinous BOT
FIGO Stage IA G1

Benign + Borderline + Malignant

Is fertility sparing surgery feasible in young patients affected by invasive ovarian cancer?

RESEARCH ARTICLE Open Access

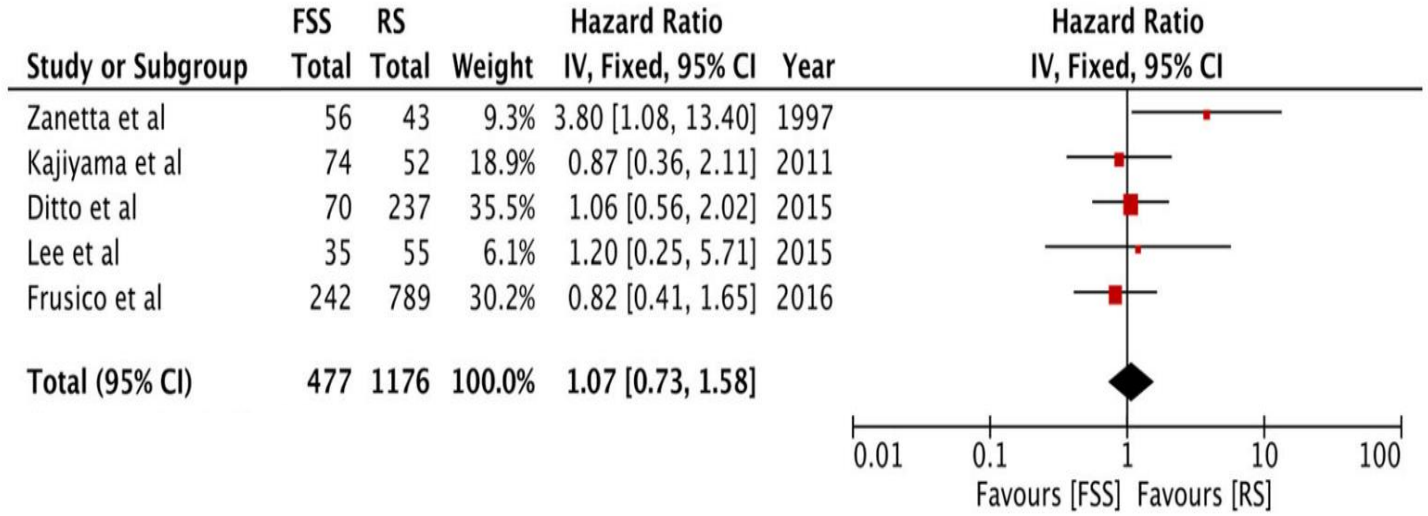
Fertility sparing surgery vs radical surgery for epithelial ovarian cancer: a meta-analysis of overall survival and disease-free survival

Denghua Liu[1], Jing Cai[2], Aiwei Gao[2], Zehua Wang[2] and Liqiong Cai[2*]

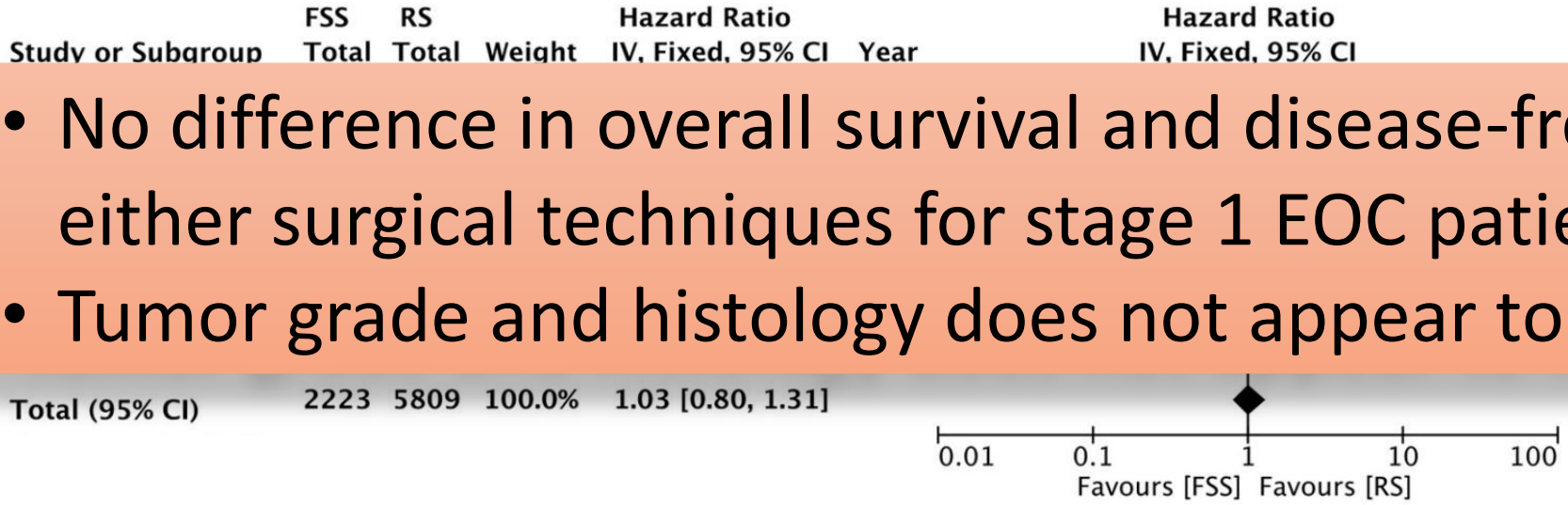
BMC Cancer 2020

Stage I Epithelial ovarian cancer

Disease-free survival FSS vs Radical Surgery



Overall Survival FSS vs Radical Surgery



- No difference in overall survival and disease-free survival with either surgical techniques for stage 1 EOC patients
- Tumor grade and histology does not appear to influence outcomes

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 30: 672–705, 2019
doi:10.1093/annonc/mdz062
Published online 2 May 2019

SPECIAL ARTICLE

ESMO–ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease†

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Recommendation: <u>FSS can be safely offered to all stage IA and IC1 low-grade ovarian carcinomas</u>.
Level of evidence: IV
Strength of recommendation: B

Recommendation: <u>there is no place for ovarian preservation for invasive EOC greater than fully staged FIGO stage I</u>.
Level of evidence: V
Strength of recommendation: A


Thank
you!