

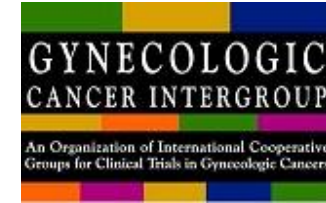
Borderline Ovarian Tumours

SURGICAL APPROACH

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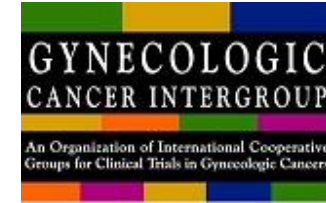
Definition 1st Challenge



- Borderline ovarian tumours (BOT): neoplasms of epithelial origin characterized by up-regulated cellular proliferation and the presence of slight nuclear atypia but without destructive stromal invasion
- Taylor (1929): “semi-malignant”
- FIGO (1971): tumours of “low malignant potential” distinct from ovarian carcinomas followed by the WHO in 1973
- Atypical proliferative tumour? ~~Tumour of low malignant potential?~~



BOT Epidemiology



- 10–15% of all epithelial ovarian malignancies
- 4.8/100,000 new cases per year
- Typical age: 40 years (up to 36% of cases occur at a younger age)
- 75% being diagnosed at FIGO stage I
- Excellent prognosis with a 10-year survival of 97% for all stages combined

BOT

Risk factors

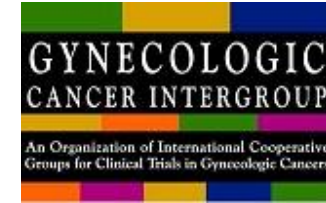
- Young
- Infertility
- HRT
- Endometriosis

Protective factors

- Contraceptive pill
- Having children
- Breast feeding



BOT Histology

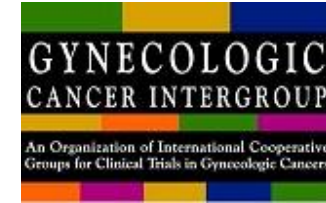


- Serous (50%): originate in ovarian cortex
 - Microinvasion
 - Micropapillary variant (up to 15%)
 - Implants are confined to the peritoneal surface without infiltration of the underlying subperitoneal fat: 30% of sBOTs

The prior subdivision of non-invasive and invasive implants has been abandoned in the recent WHO classification, and any invasive foci are now considered peritoneal LGSC reflecting their similar biologic behaviour.



BOT Histology

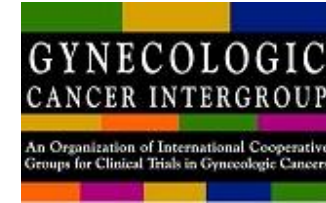


- Mucinous (40%): $\geq 10\%$ of the epithelial volume must demonstrate increased proliferation with papillary infoldings or pseudostratification and mild to moderate nuclear atypia
 - Microinvasion (4 to 18%): stromal invasion measuring < 5 mm

No single criterion allows definitive differentiation of primary versus metastatic ovarian mucinous tumours, features favouring metastases include smaller size < 10 cm, bilaterality, surface involvement, (multi)nodular growth pattern, extra-ovarian disease, and associated pseudomyxoma ovarii or pseudomyxoma peritonei.



BOT Histology

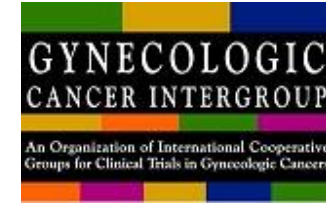


- Transitional cell/Brenner tumours (<3%)
 - Seromucinous (5%): formerly endocervical or mullerian
 - Endometrioid (2%): 39% have at least synchronous endometrial hyperplasia
 - Clear cell (<1%)
- } Endometriosis



BOT

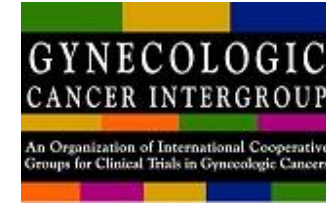
Diagnosis – the next challenge!



- Symptoms: abdominal (80%) like distension or pain, GI, urinary
- Tumour markers: CA125, CEA, CA199
- Imaging: Ultrasound, MRI, CT, CT PET



Diagnosis Ultrasound



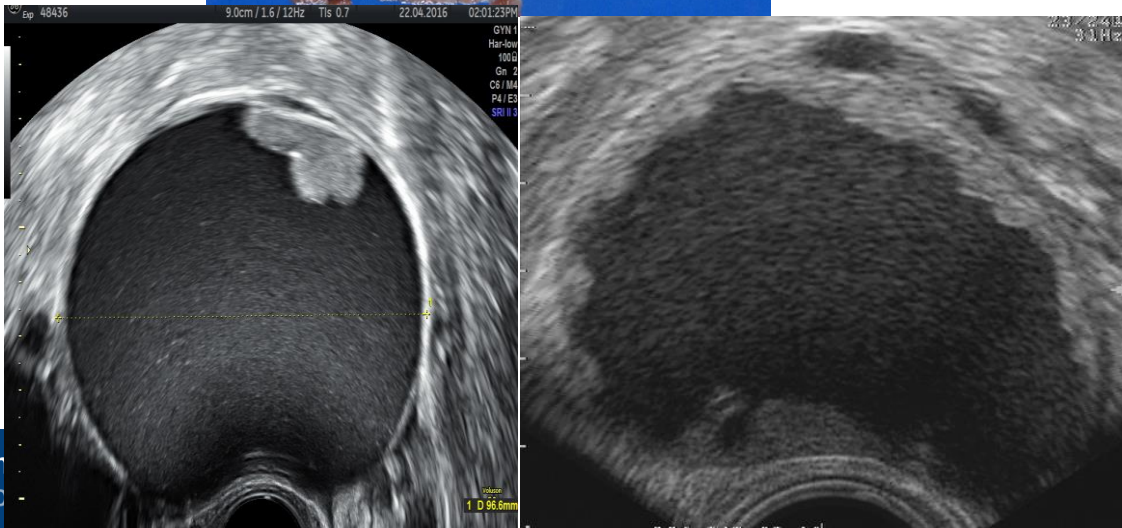
- Serous / seromucinous BOT: positive ovarian crescent sign, unilocular cyst with extensive papillaries arising from the inner wall
- Mucinous BOT: well defined multilocular nodule (Honeycomb nodule) arising from the cyst wall or suspended within the cyst cavity, thick echogenic fluid content

Exacoustos et al 2005

Fruscella et al 2005

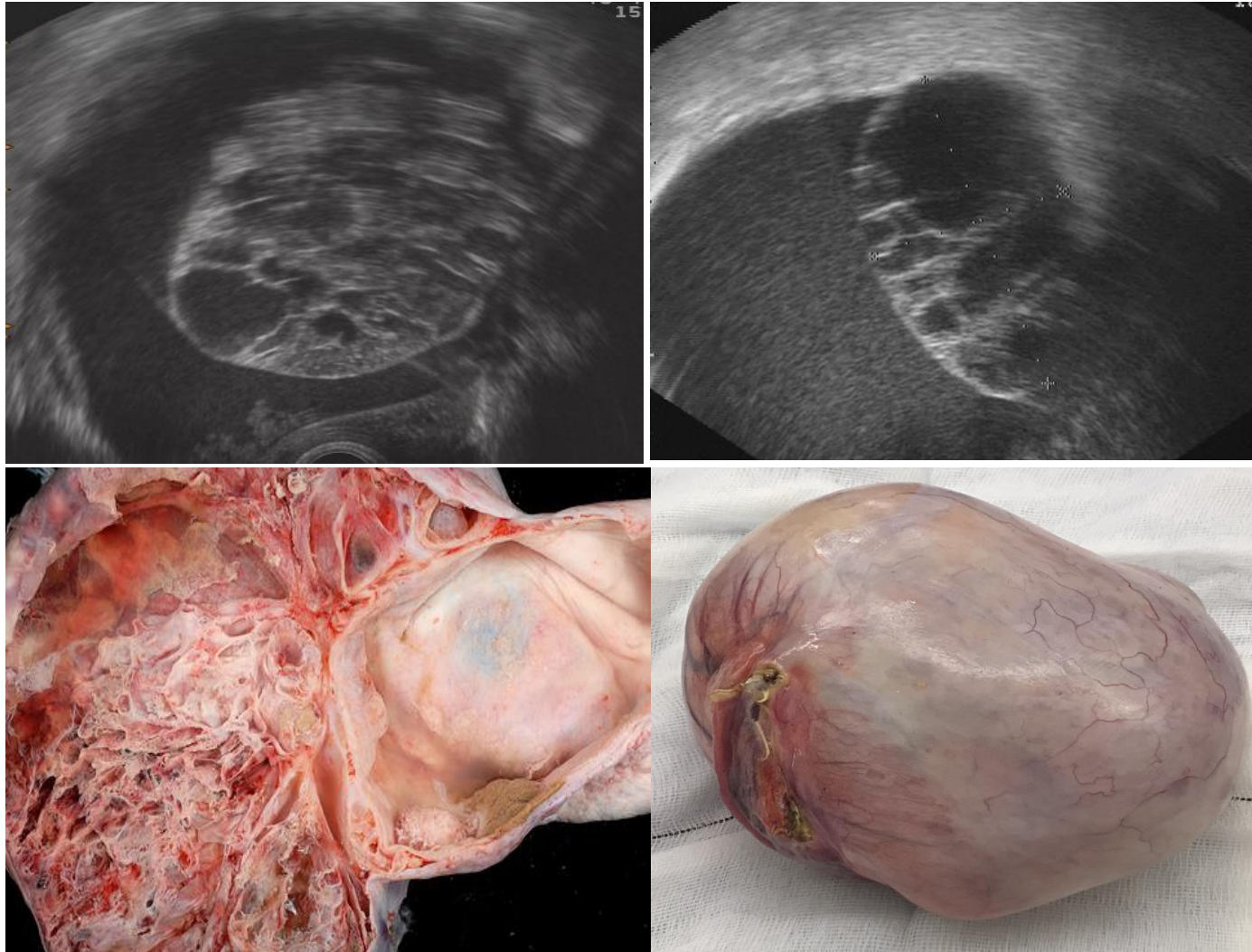
Yazbek et al 2007

BOT– serous / seromucinous



Borderline ovarian tumour

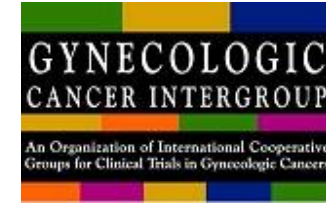
Mucinous GI type





Borderline Ovarian Tumours

Pattern recognition



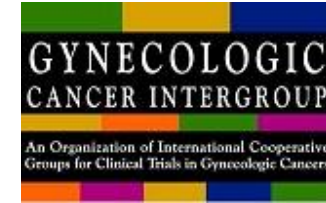
- Ultrasound diagnosis of BOT is highly specific
- Typical features are absent in one third of cases, which are typically misdiagnosed as benign lesions
- Pre-operative ultrasound examination may help to offer more conservative treatment to younger women with borderline ovarian tumours

Yazbek et al., 2007

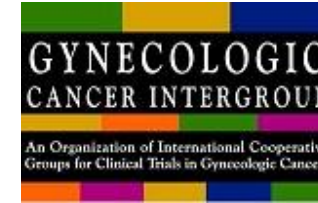


BOT

Treatment – another challenge



- Standard treatment?: complete surgical resection and surgical staging including omentectomy, peritoneal biopsies, cytology of peritoneal washings, and appendicectomy in case of mucinous BOT
- Radical approach: TAH, BSO + standard staging
- 27–54% of patients <40 year old – Fertility preservation required



BOT

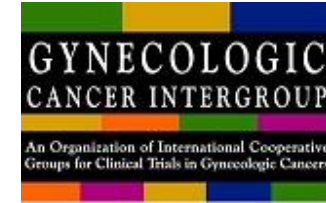
Treatment – selection criteria?

- Fertility preservation
 - <40 years
 - Want to preserve fertility
 - Committed to exhaustive follow-ups
 - No invasive implants
- Radical approach
 - >40 years
 - Childbearing desires completed
 - Would find it difficult to adhere to follow-up requirements
 - Invasive implants



BOT

Radical approach

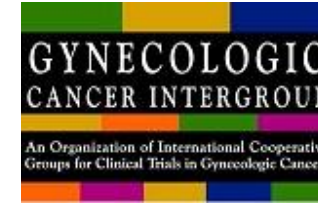


- Recurrence rate 3-5%
- No significant role for pelvic and paraaortic lymphadenectomy
 - Survival not affected by either involvement of lymph nodes or resection of the nodes (Lesieur 2011)
 - selective lymphadenectomy to those with increased risk of lymph node metastasis? Based on a univariate analysis: black ethnicity, T1b and T1c stages, serous histology, and tumor size > 5 cm (Matsuo 2017)
- No role for chemotherapy (Gokcu 2016)
- HRT esp. in the premenopausal group

BOT

Fertility Preservation Surgery

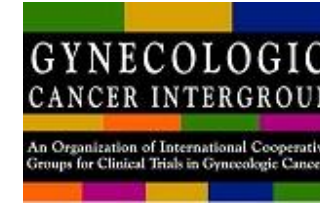




BOT

Fertility Preservation Surgery

- The cumulative pregnancy rate is 55.7%: 45.4% for USO and 40.3% for cystectomy
- Counsel about subfertility: loss of ovarian reserve and adhesions (10-35%)
- Cystectomy in unilateral serous BOT is significantly associated with a higher recurrence rate, albeit no impact on survival can be demonstrated (Vasconcelos and Mendes 2015)
- USO is advisable in the case of mucinous BOT due to high risk of recurrence as carcinoma if cystectomy done (Koskas 2011).
- A more conservative approach (bilateral ovarian cystectomy) should be definitively favoured in bilateral BOT, which is almost always serous, because no significant difference is seen in terms of recurrence rate when compared to USO + contralateral cystectomy



Fertility Preservation Surgery

Oncological outcomes

Type of surgery	N	Recurrence total N (%)	Recurrence BOT N (%)	Recurrence invasive N (%)
Cystectomy	288	53 (18.4)	48 (91)	5 (9)
USO	658	64 (9.7)	60 (94)	4 (6)

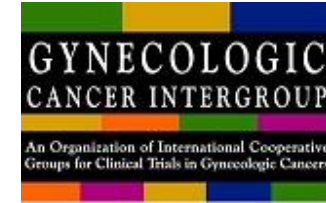
Total recurrence 117/946 (12.3%)

Alvarez & Vazquez-Vicente 2015



BOT

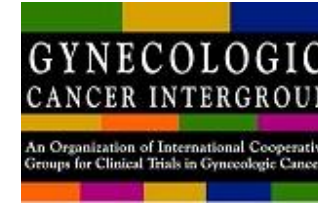
Risk of recurrence



- Higher stage
- Incomplete staging
- Each skipped surgical step: omentectomy, peritoneal biopsies, cytology
- Tumour residuals
- Organ preservation
- Young age

du Bois 2013
Trillsch 2014
Trillsch 2015

} (AGO)
ROBOT
study

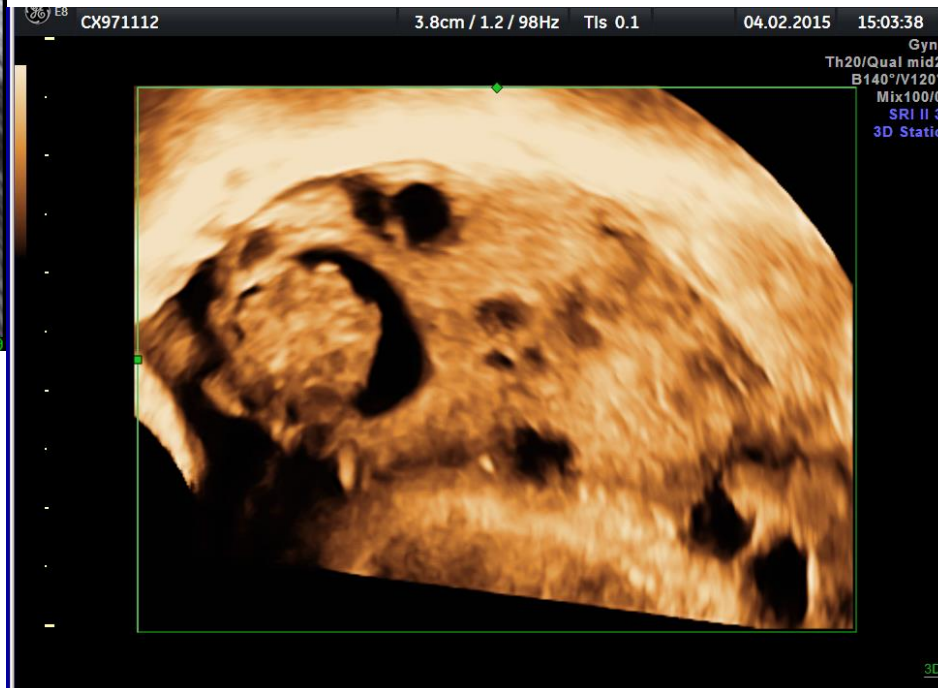
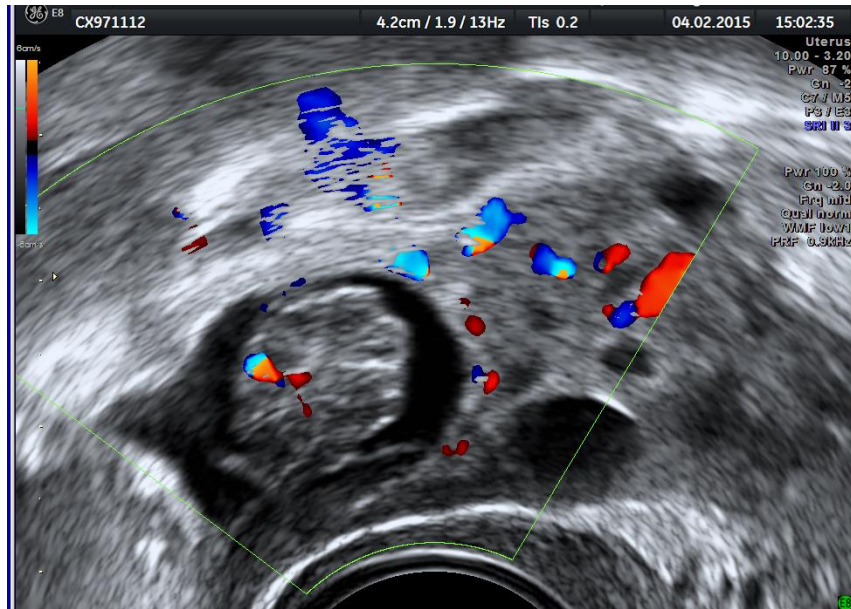
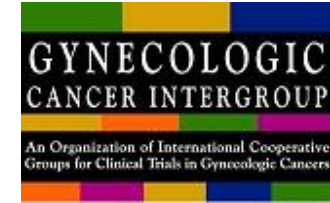


Laparoscopy or Laparotomy

- Laparoscopy: reserve to masses ≤ 5 cm (Maneo et al 2004)
- Laparoscopic ovarian cystectomy could lead to higher relapse rates as compared with laparotomy, because of the increased risk of cyst rupture (14.9% versus 7.7%), incomplete staging, cellular dissemination, and increased trocar scarring [Troppe 2012].
- Benefits of laparoscopy: lower morbidity, fewer postsurgical adhesions, less pain and a shorter hospital stay [Desfeux 2006]

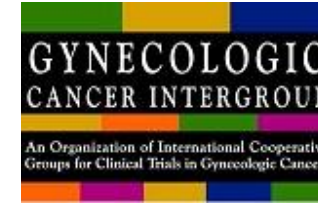


BOT
Recurrent serous



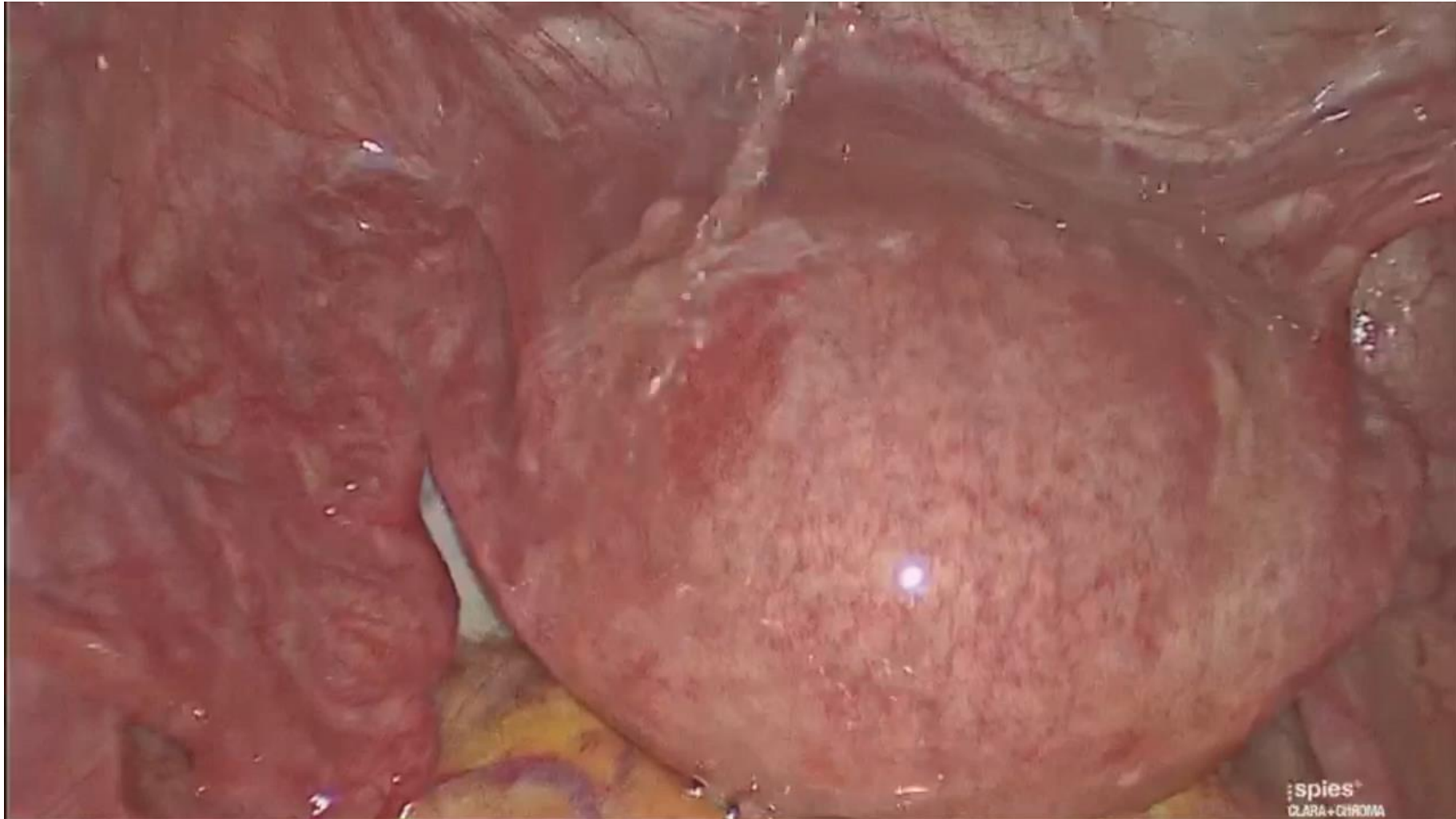


Recurrent sBOT One more challenge!



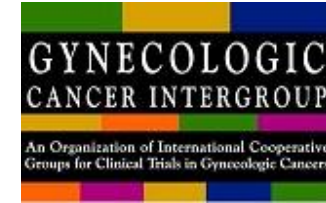
- Franchi et al 2016: assessed the growth rate by longitudinal follow up every 3 months until clinical settings advised on surgery (cyst >4cm, doubled in size, anxiety)
 - All recurrences were BOTs
 - Slow growth rate
 - Safety and feasibility of expectant management (up to 5 years)
- Jones et al 2017: assessed the use of intraoperative ultrasound guidance for treatment of recurrent sBOT for tumours with median diameter of 18mm.
 - All recurrences were BOTs
 - Complete tumor excision
 - Minimizing the removal of healthy ovarian tissue

Recurrent serous BOT





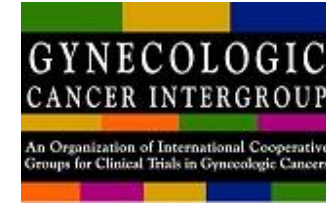
BOT Follow up



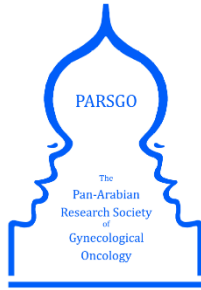
- 25% of recurrence diagnosed >5 years up to 15 years (Romeo 2013)
- Our Centre:
 - Dedicated one stop ovarian clinic: ultrasound, serum tumour markers (esp. if previously raised)
 - Every 4 months first 2 years
 - Every 6 months 3rd year
 - Every year thereafter (indefinitely for now)



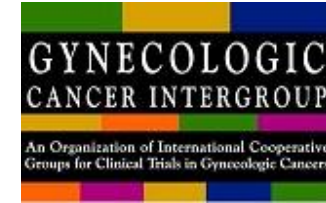
Completion surgery Is it necessary?



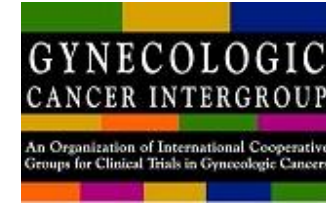
- Removal of ovary(ies) and tube(s)
- Hysterectomy not required (no recurrence has been observed in uterus)
- Should it be offered only to patients with high risk of recurrence
- Timing?



BOT Counselling

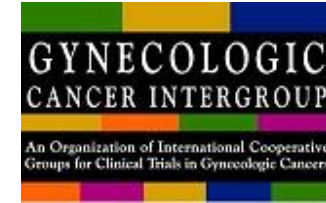


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- Diagnostic accuracy
 - Radical vs fertility preservation
 - Risk of recurrence and ways of management
 - Low risk of transformation into invasive malignancy
 - Long term follow up



Future work

- Diagnosis
- RCTs:
 - radical vs conservative surgery
 - laparoscopy vs laparotomy
- Completion surgery after completed family planning: a prospective registry?
- RCTs: the benefit of adjuvant therapy with optimally dosed chemotherapy and newer targeted drugs are necessary, particularly for advanced borderline ovarian tumours



Summary

- Borderline ovarian tumours carry a good overall prognosis
- Diagnostic and pathologic challenges
- Fertility preservation is associated with a higher risk of disease relapse; but overall survival is not compromised
- Recurrence could happen after 15 years of initial diagnosis
- Establish an international consensus to standardize the surgical management in BOTs



Thank you.

