

# Gynecological cancer

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**DEBRECENI  
EGYETEM**





## Globocan 2020

Site	Incidence (% of all sites)	Mortality (% of all sites)
Breast	2,261,419 (11,7)	684,996 (6,9)
Lung	2,206,771 (11,4)	1,796,144 (18,0)
Cervix	604,127 (3,1)	341,831 (3,4)
Corpus	417,367 (2,2)	97,370 (1,0)
Ovary	313,959 (1,6)	207,252 (2,1)
Vulva	45,240 (0,2)	17,427 (0,2)

# Cervical cancer pathogenesis

Oncogenic HPV subtypes  
HPV-DNA integrated into host DNA  
E6 protein suppresses p16/p53 genes  
E7 protein suppresses Rb gene



# Prognostic factors

- TNM and FIGO stages, tumor-size, extracervical spread, lymphatic spread
- Histological type, grade
- Depth of stromal invasion, unaffected stromal thickness
- LVI
- Distant spread



# Clinical and radiological work-up

- Pelvic examination and biopsy
- Pelvic MRI
- Vaginal  $\pm$  rectal US
- Chest and abdominal CT or whole body PET-CT
- Cystoscopy or rectoscopy if bladder or rectum suspicious for spread



# FIGO-2018 Staging of cervical cancer



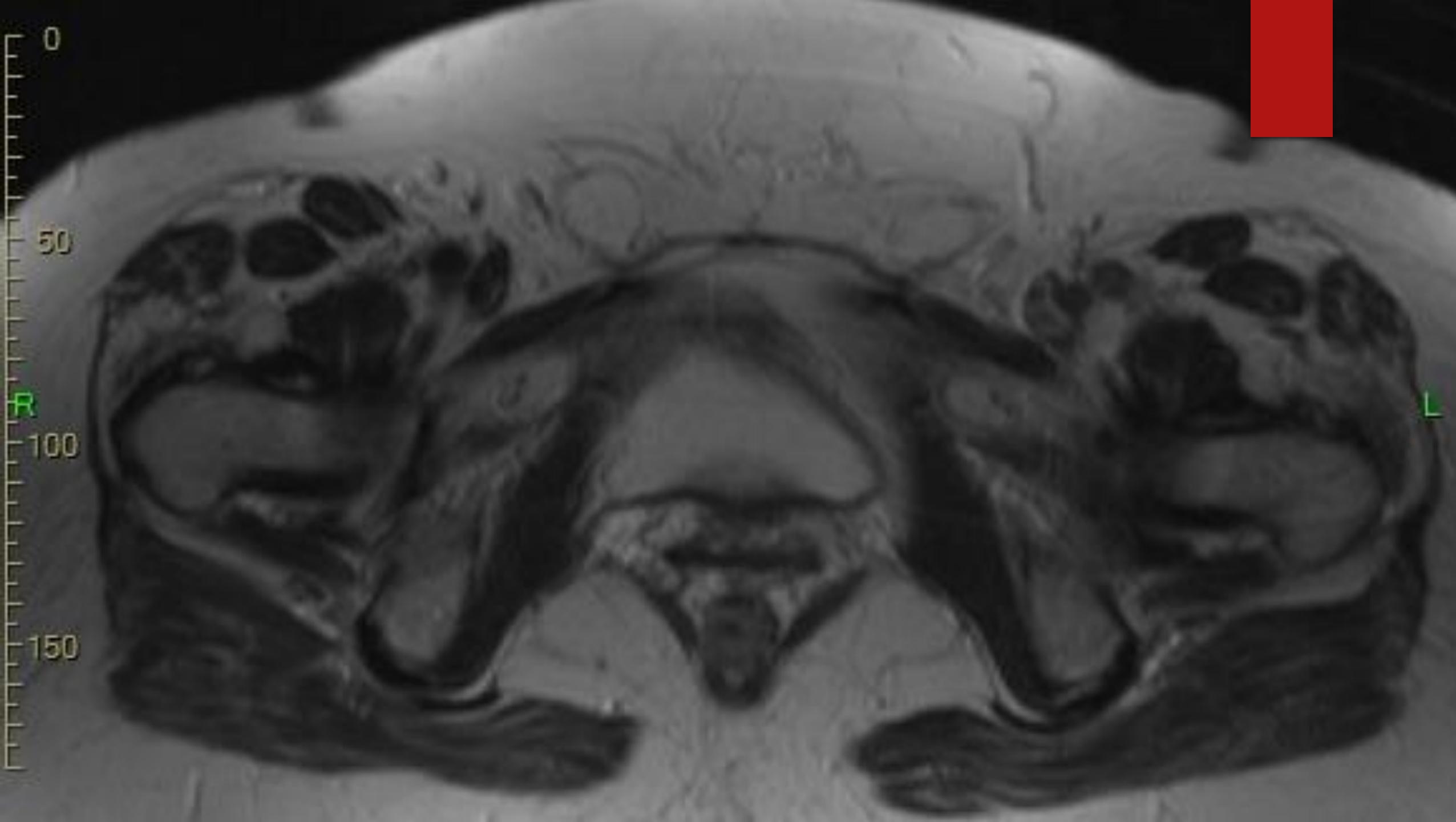
- IA1 <3mm stromal invasion
- IA2  $\geq$ 3mm to <5mm stromal invasion
- IB1 <2cm tumor-site and  $\geq$ 5mm stromal invasion
- IB2  $\geq$ 2cm and <4cm tumor-size
- IB3  $\geq$ 4cm tumor-size
- IIA1 <4cm tumor-size with extrauterine spread without spread tp parametrium and lower-third vagina
- IIA2  $\geq$ 4cm tumor-size with extrauterine spread without spread tp parametrium and lower-third vagina

## **FIGO-2018 Staging of cervical cancer cont'd**

- IIB Parametrial spread not reaching the pelvic side-wall
- IIIA Lower-third vaginal spread and parametrial spread not reaching the pelvic side-wall
- IIIB Parametrial spread reaching the pelvic side-wall or hydronephrosis not explained by other cause
- IIIC1 Pelvic lymph-node metastasis, IIIC1r if only radiological finding
- IIIC2 Paraaortic lymph-node metastasis, IIIC2r if only radiological finding
- IVA Pelvic extragenital organ affected
- IVB Distant metastasis







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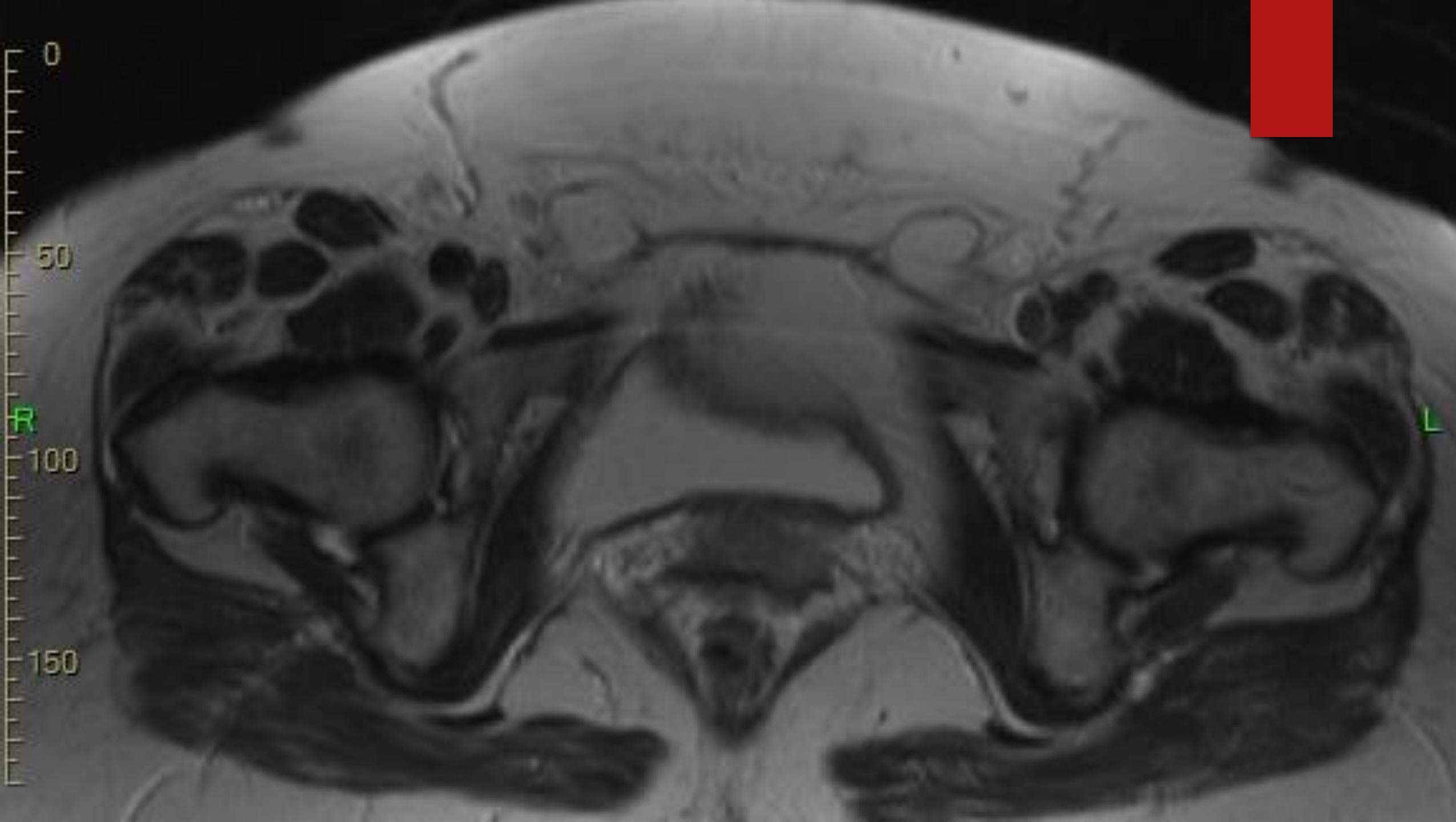
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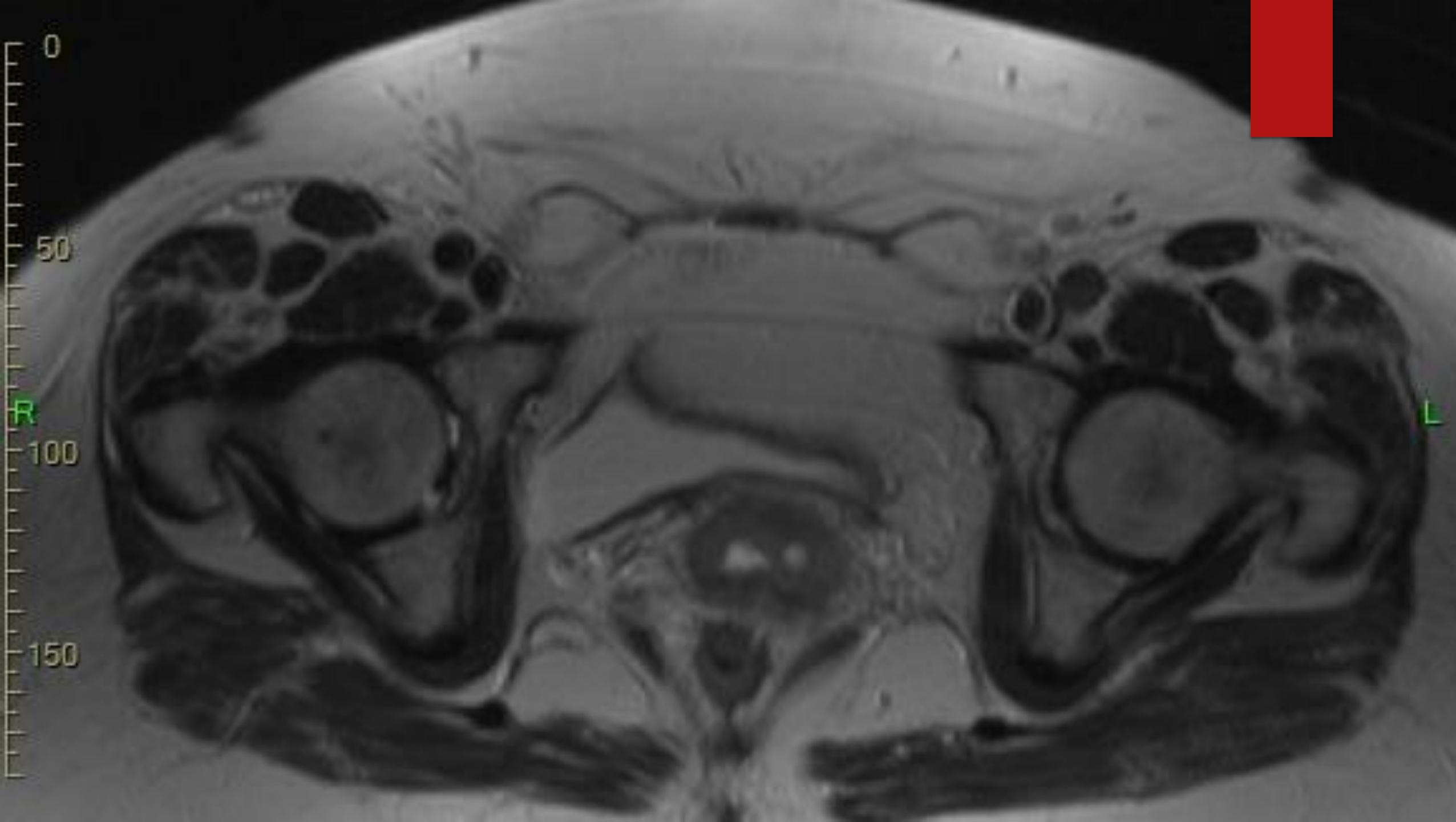
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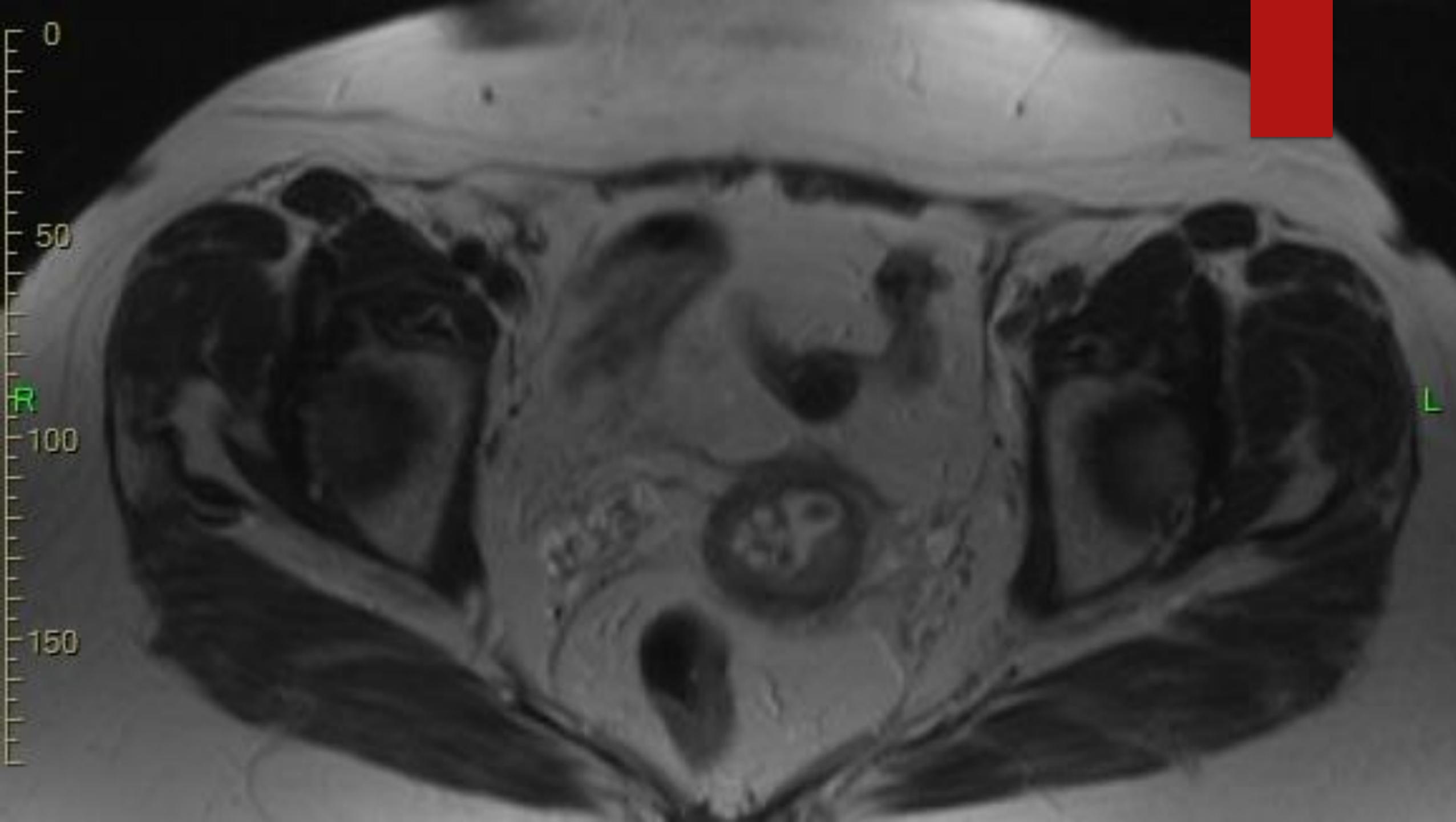
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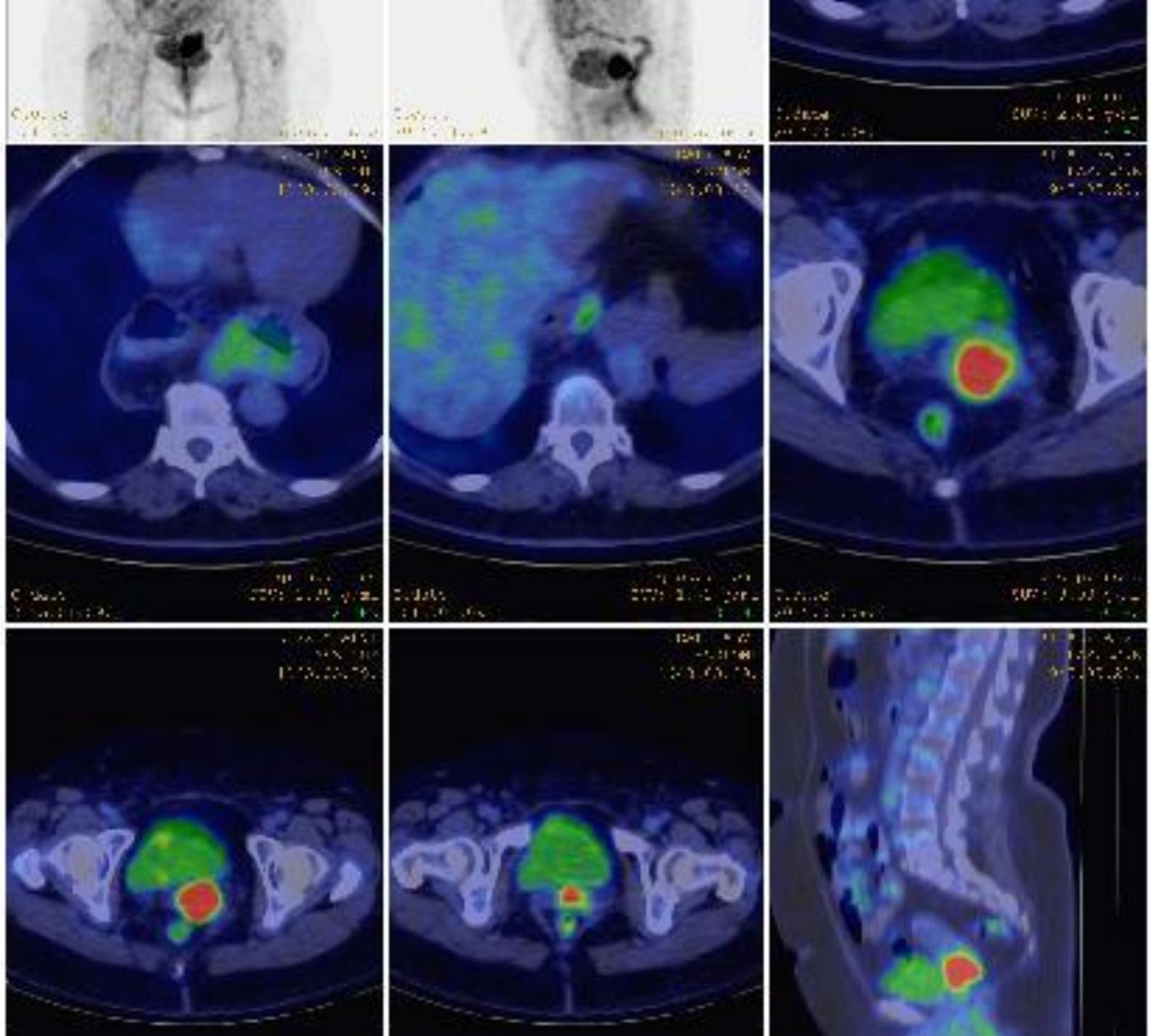
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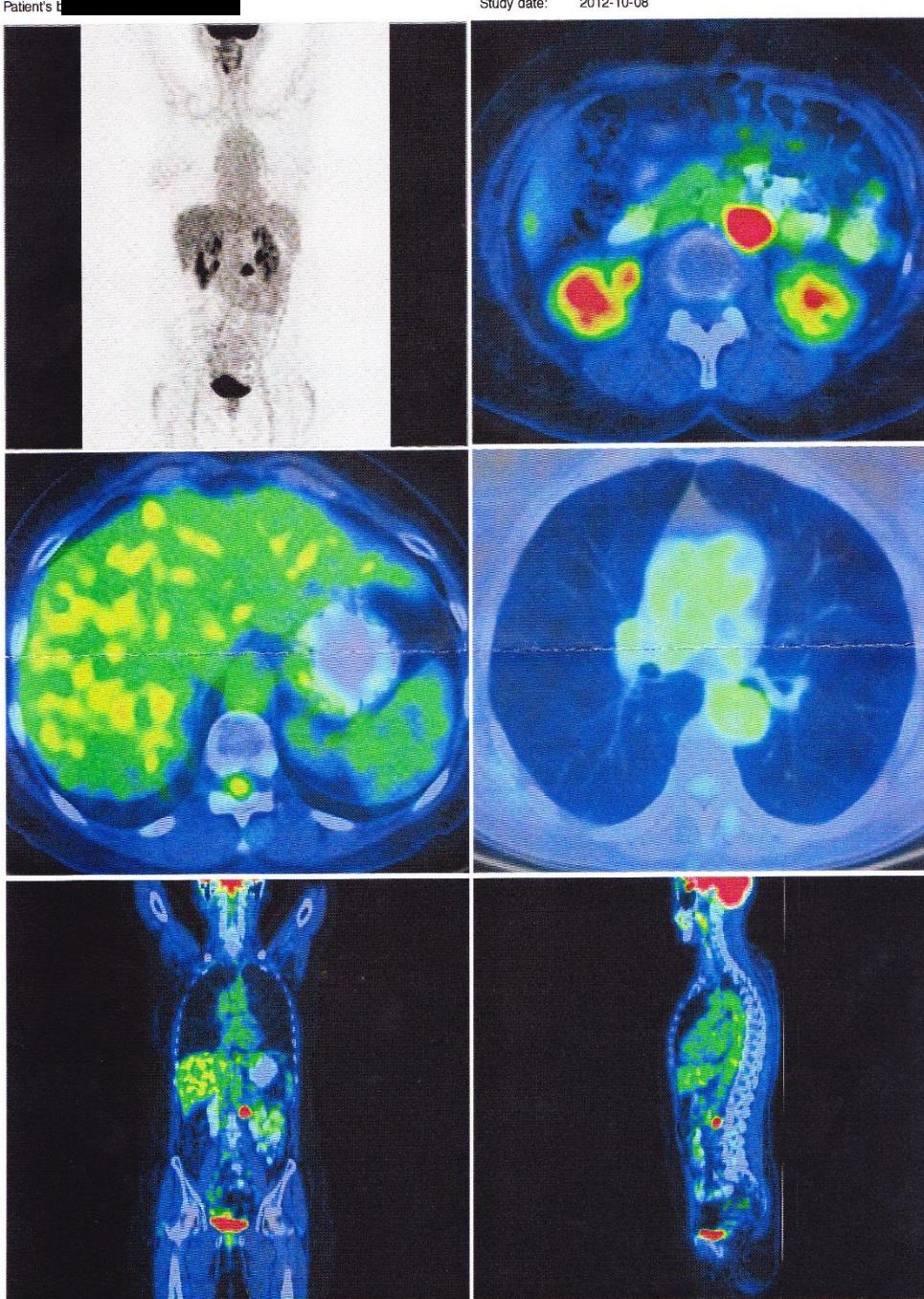
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InterView Fusion - 1.08.009.0000 BETA

Acquisition date: 2012-10-08

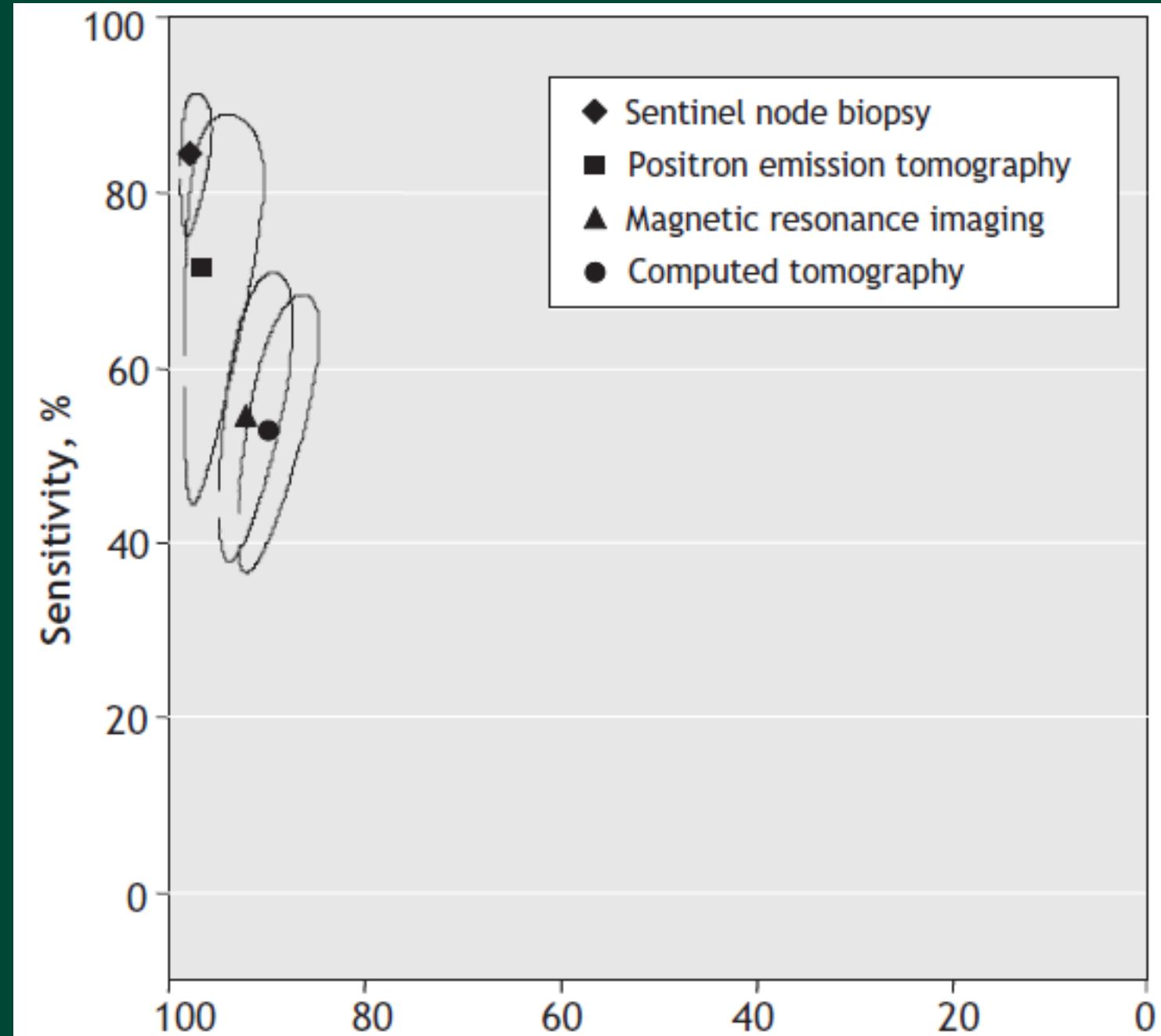
2012.10.09.15.51

Page 1

25 cm



Selman et al.  
CMAJ 2008;178(7):855-62



# Cervical cancer treatment



Early stages

Locally advanced disease

Advanced disease

Surgical Tx

Chemoradiotherapy

Chemotherapy

Investigational modalities

Neoadjuvant chemotherapy

Checkpoint inhibitors

Thyrosinkinase inhibitors

Antigen-loaded dendritic cells

# Radical surgery adjusted to prognostic features

**Table 2. Risk groups according to prognostic factors: suggested type(s) of radical hysterectomy**

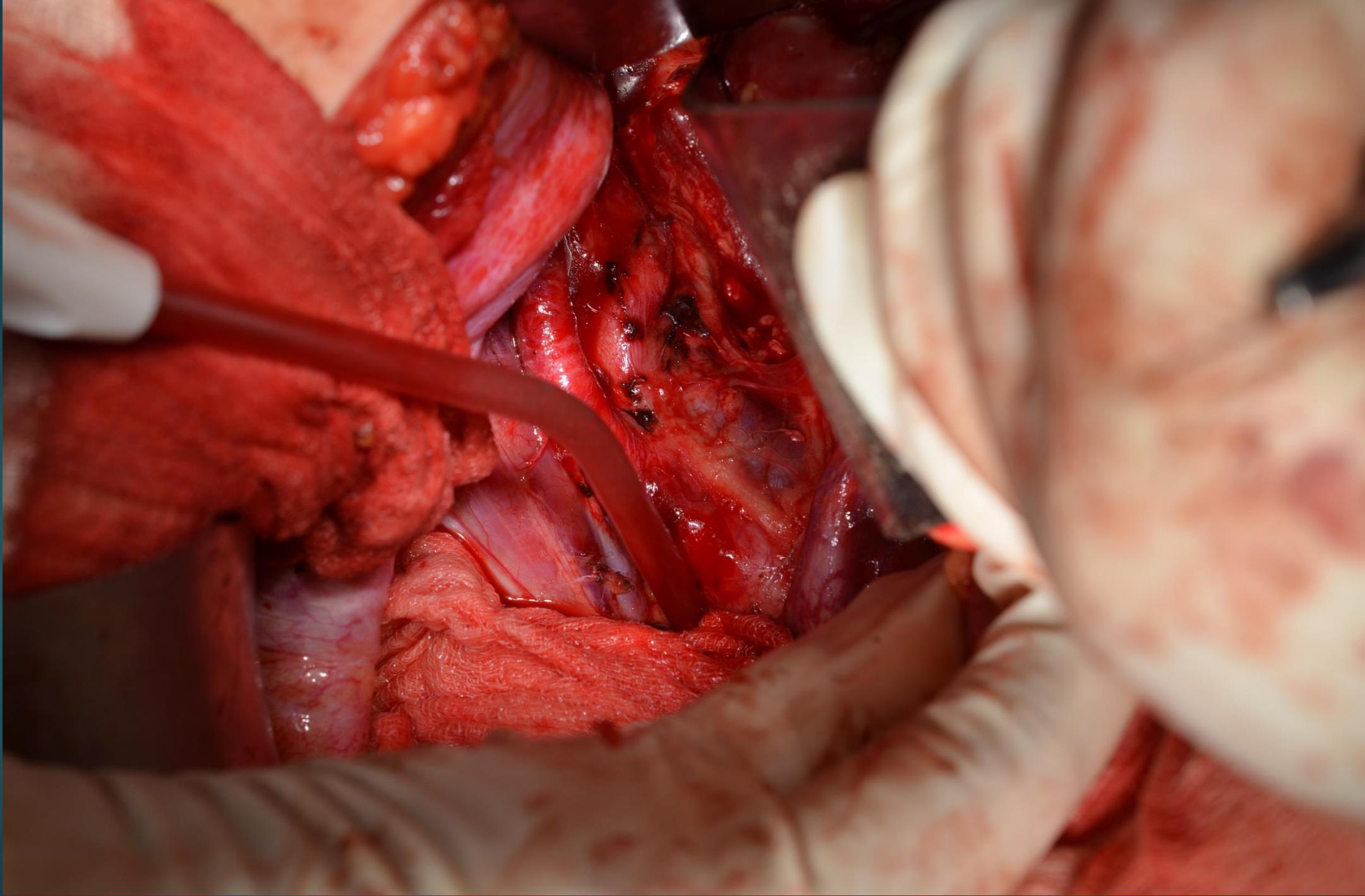
Risk group	Tumour size	LVSI	Stromal invasion	Type of radical hysterectomy*
Low risk	< 2 cm	Negative	Inner 1/3	B1 (A)
Intermediate risk	≥ 2 cm	Negative	Any	B2 (C1)
	< 2 cm	Positive	Any	
High risk	≥ 2 cm	Positive	Any	C1 (C2)

\* according to the Querleu-Morrow classification (see table 3)

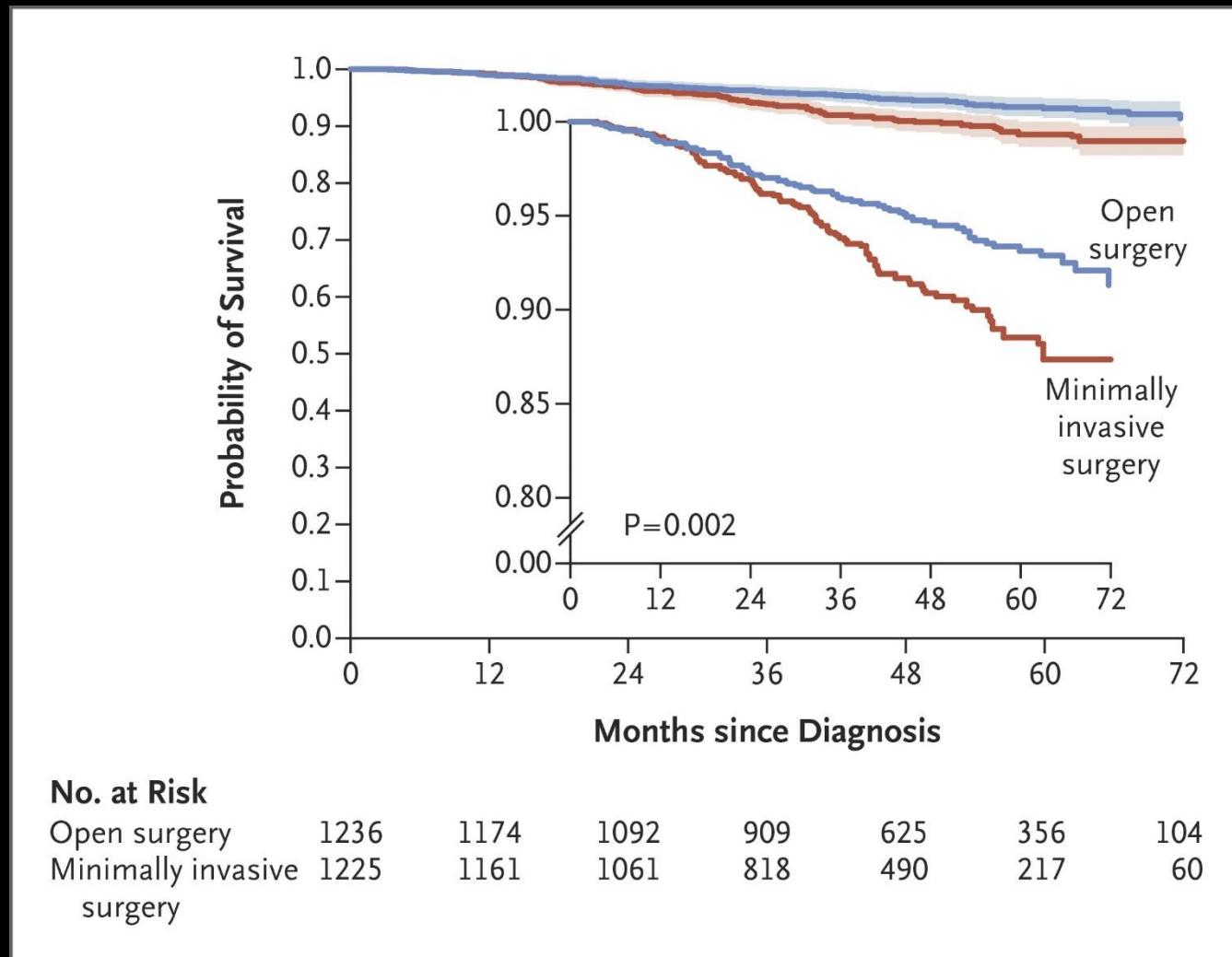


**Table 3. Querleu-Morrow classification<sup>5</sup>**

Type of radical hysterectomy	Paracervix or lateral parametrium	Ventral parametrium	Dorsal parametrium
Type A	Halfway between the cervix and ureter (medial to the ureter-ureter identified but not mobilised)	Minimal excision	Minimal excision
Type B1	At the ureter (at the level of the ureteral bed—ureter mobilised from the cervix and lateral parametrium)	Partial excision of the vesicouterine ligament	Partial resection of the rectouterine-rectovaginal ligament and uterosacral peritoneal fold
Type B2	Identical to B1 plus paracervical lymphadenectomy without resection of vascular/nerve structures	Partial excision of the vesicouterine ligament	Partial resection of the rectouterine-rectovaginal ligament and uterosacral fold
Type C1	At the iliac vessels transversally, caudal part is preserved	Excision of the vesicouterine ligament (cranial to the ureter) at the bladder. Proximal part of the vesicovaginal ligament (bladder nerves are dissected and spared)	At the rectum (hypogastric nerve is dissected and spared)
Type C2	At the level of the medial aspect of iliac vessels completely (including the caudal part)	At the bladder (bladder nerves are sacrificed)	At the sacrum (hypogastric nerve is sacrificed)
Type D	At the pelvic wall, including resection of the internal iliac vessels and/or components of the pelvic sidewall	At the bladder. Not applicable if part of exenteration	At the sacrum. Not applicable if part of exenteration



**Inverse Probability of Treatment-Weighted Survival Curves among Women with Stage IA2 or IB1 Cervical Cancer, According to Type of Surgery.**

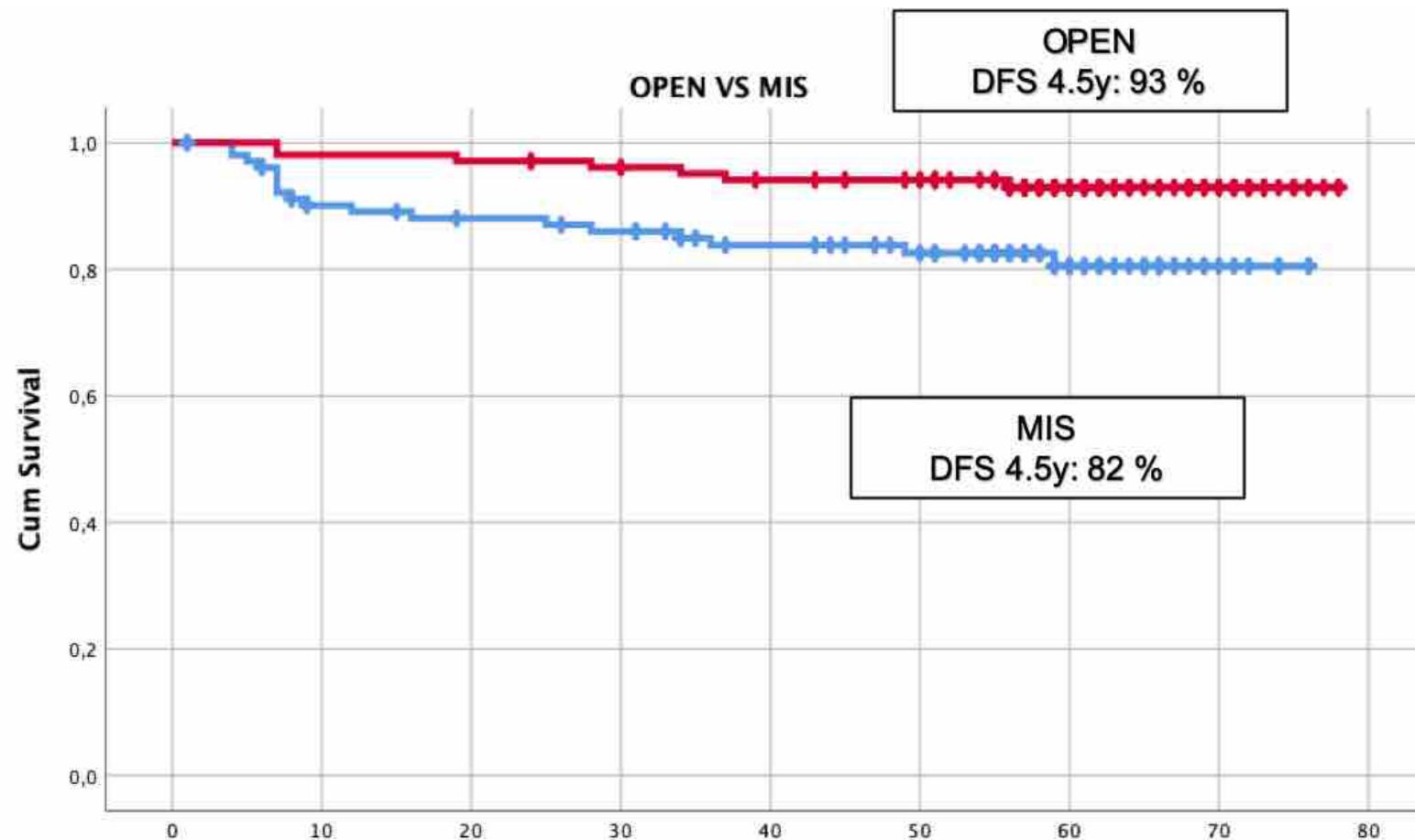


Melamed A et al. N Engl J Med 2018;379:1905-1914



The NEW ENGLAND  
JOURNAL of MEDICINE

# SUCCOR study of radical hysterectomies of 2013-2014 in ESGO area for cx IB1(FIGO2009)

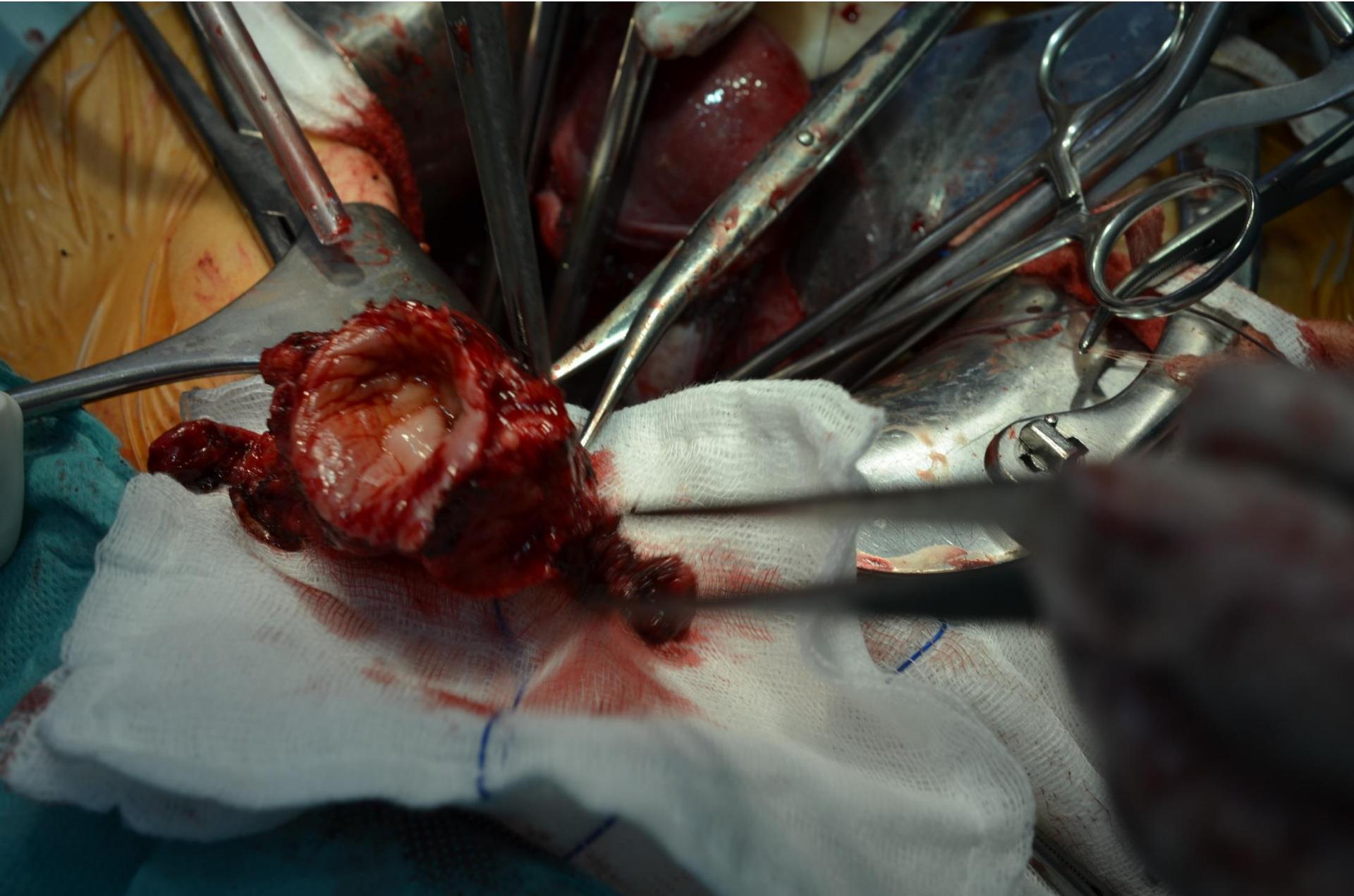


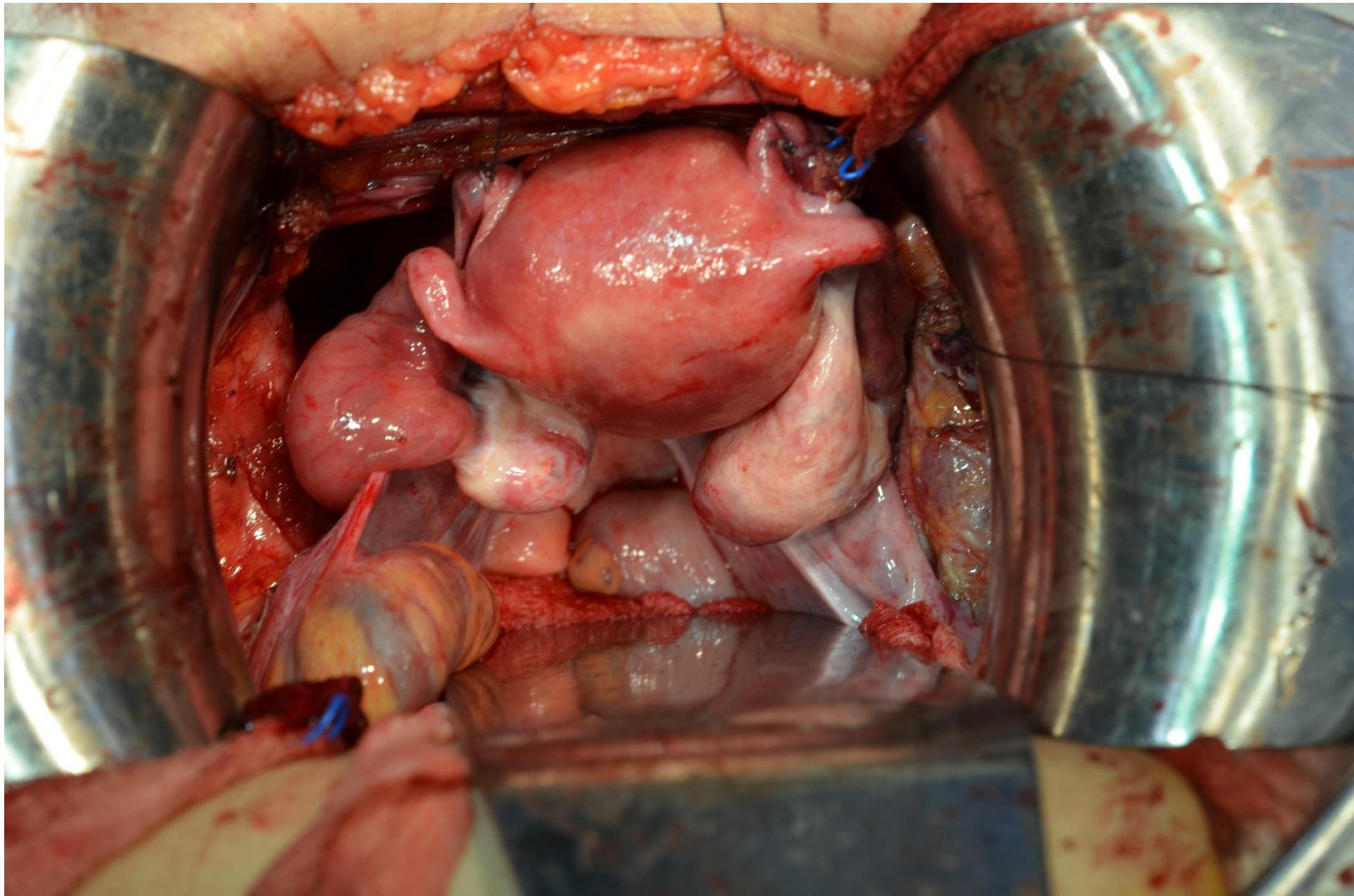
**DEBRECENI  
EGYETEM**

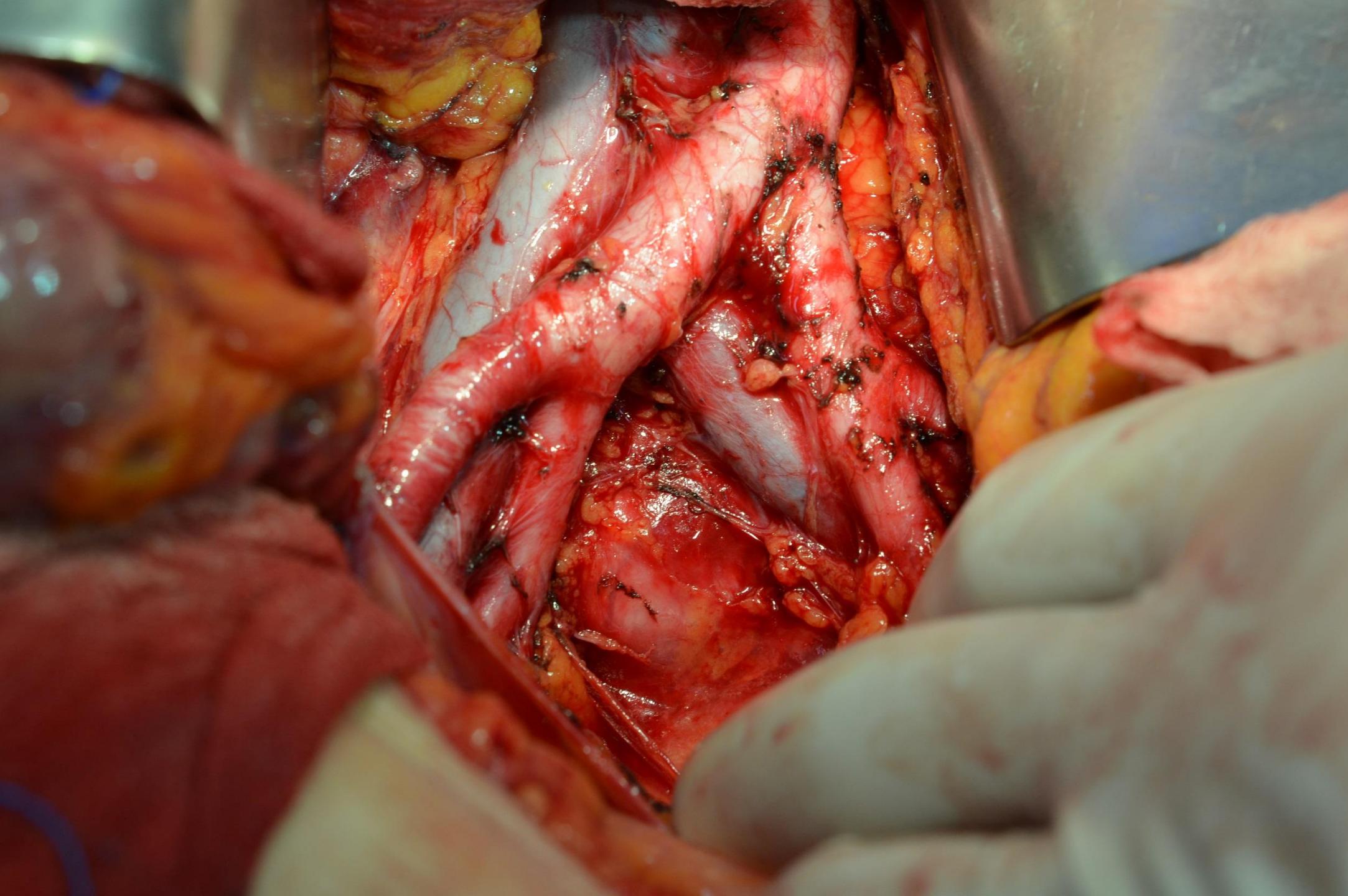
# Prerequisites of fertility preserving radical trachelectomy

- Family planning
- Gynecological oncology center
- Complete exploration of prognostic features
- <T1B1 SSC or HPV-associated adenocarcinoma
- Unaffected cervix assessed by expert MRI
- Radiologically and histologically unaffected lymph-nodes, assessed preferably by sentinel ultrastaging





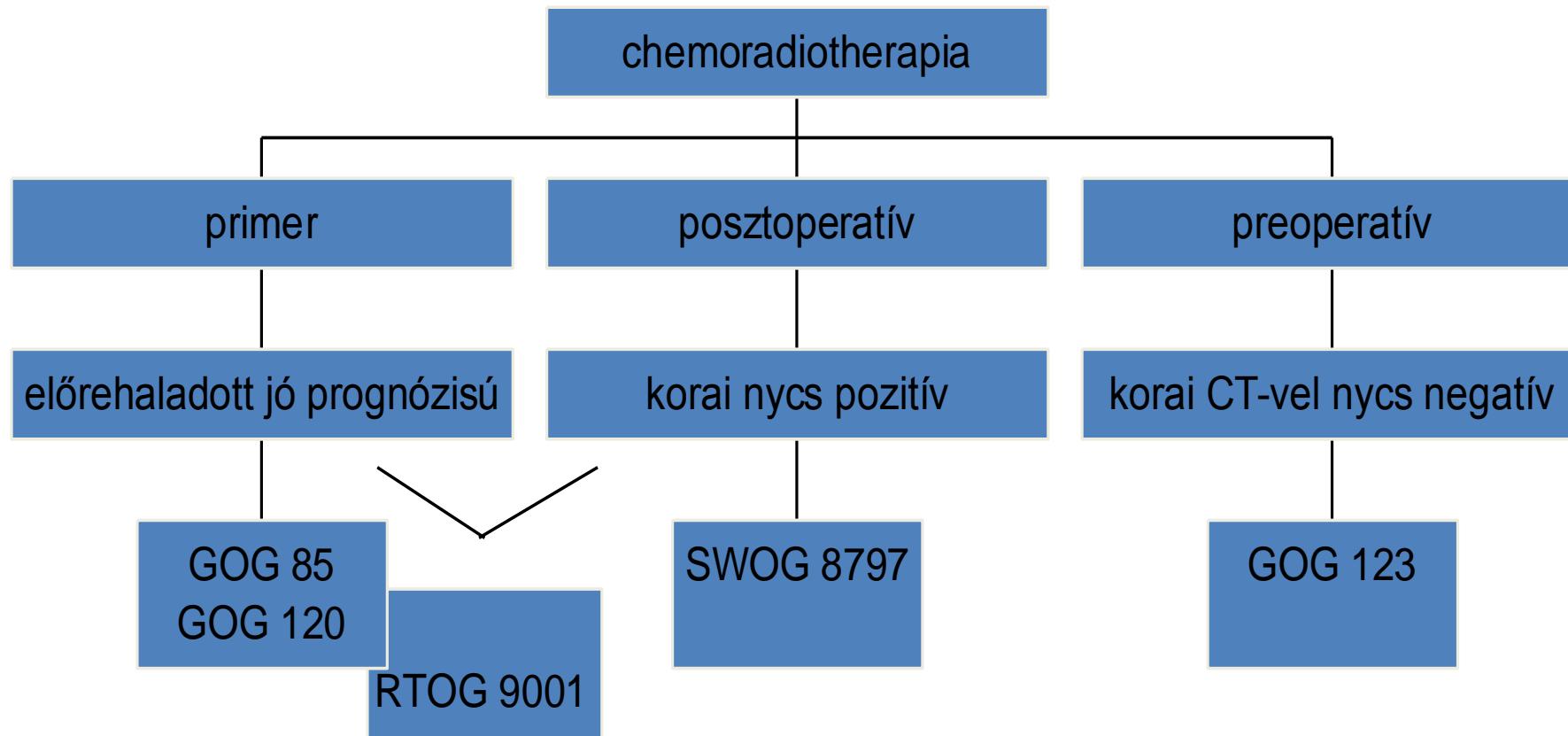




# Sedlis-criteria of postop. raditherapy

LVSI	Stromal-invasion	Tumor-size
+	Inner 1/3	Any
+	Medial 1/3	<u>&gt;2cm</u>
+	Superficial 1/3	>5cm
-	Medial of inner 1/3	<u>&gt;4cm</u>

## cervix carcinoma



**Original Article**

# **Improved Survival with Bevacizumab in Advanced Cervical Cancer**

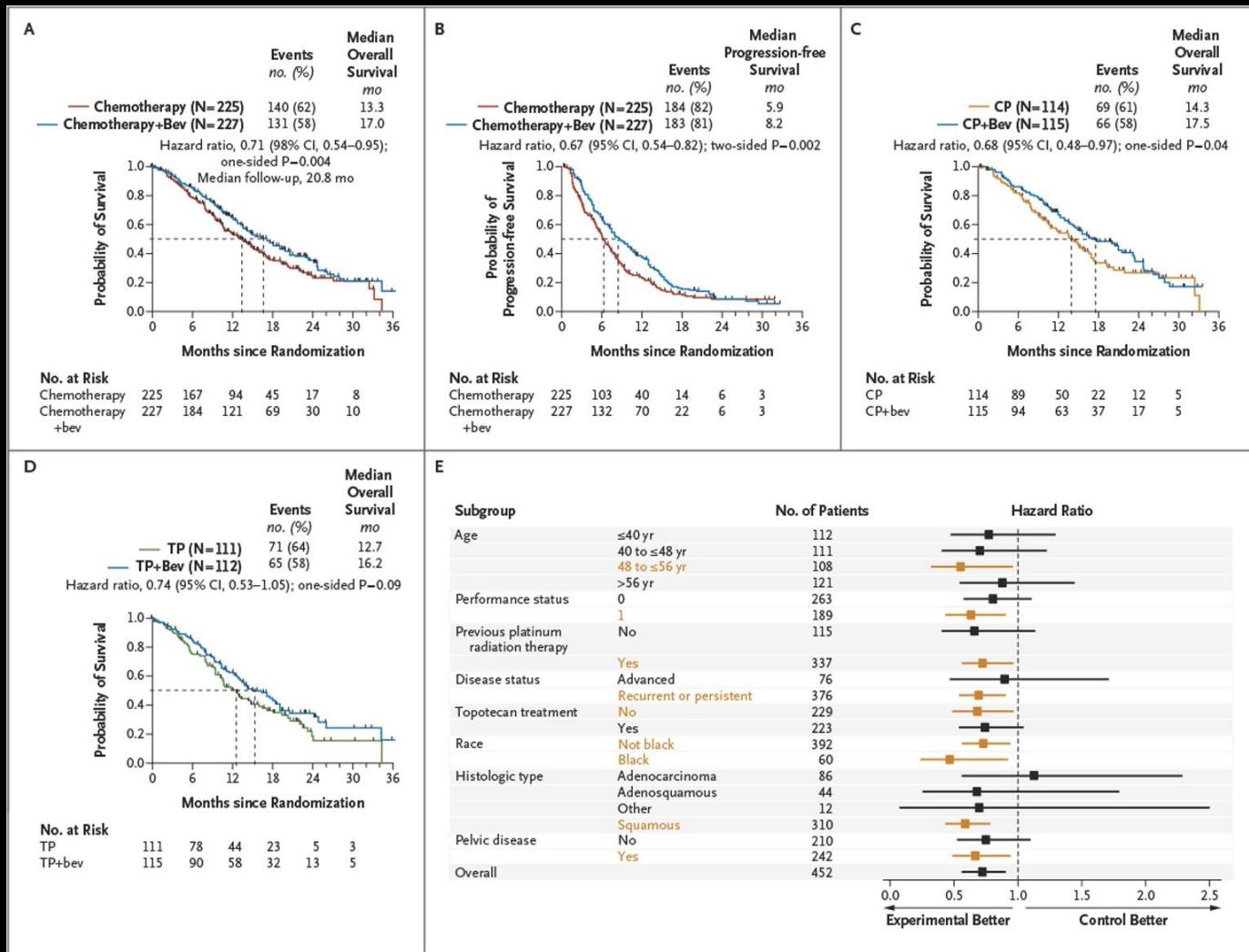
Krishnansu S. Tewari, M.D., Michael W. Sill, Ph.D., Harry J. Long, III, M.D., Richard T. Penson, M.D., Helen Huang, M.S., Lois M. Ramondetta, M.D., Lisa M. Landrum, M.D., Ana Oaknin, M.D., Thomas J. Reid, M.D., Mario M. Leitao, M.D., Helen E. Michael, M.D., and Bradley J. Monk, M.D.

N Engl J Med  
Volume 370(8):734-743  
February 20, 2014



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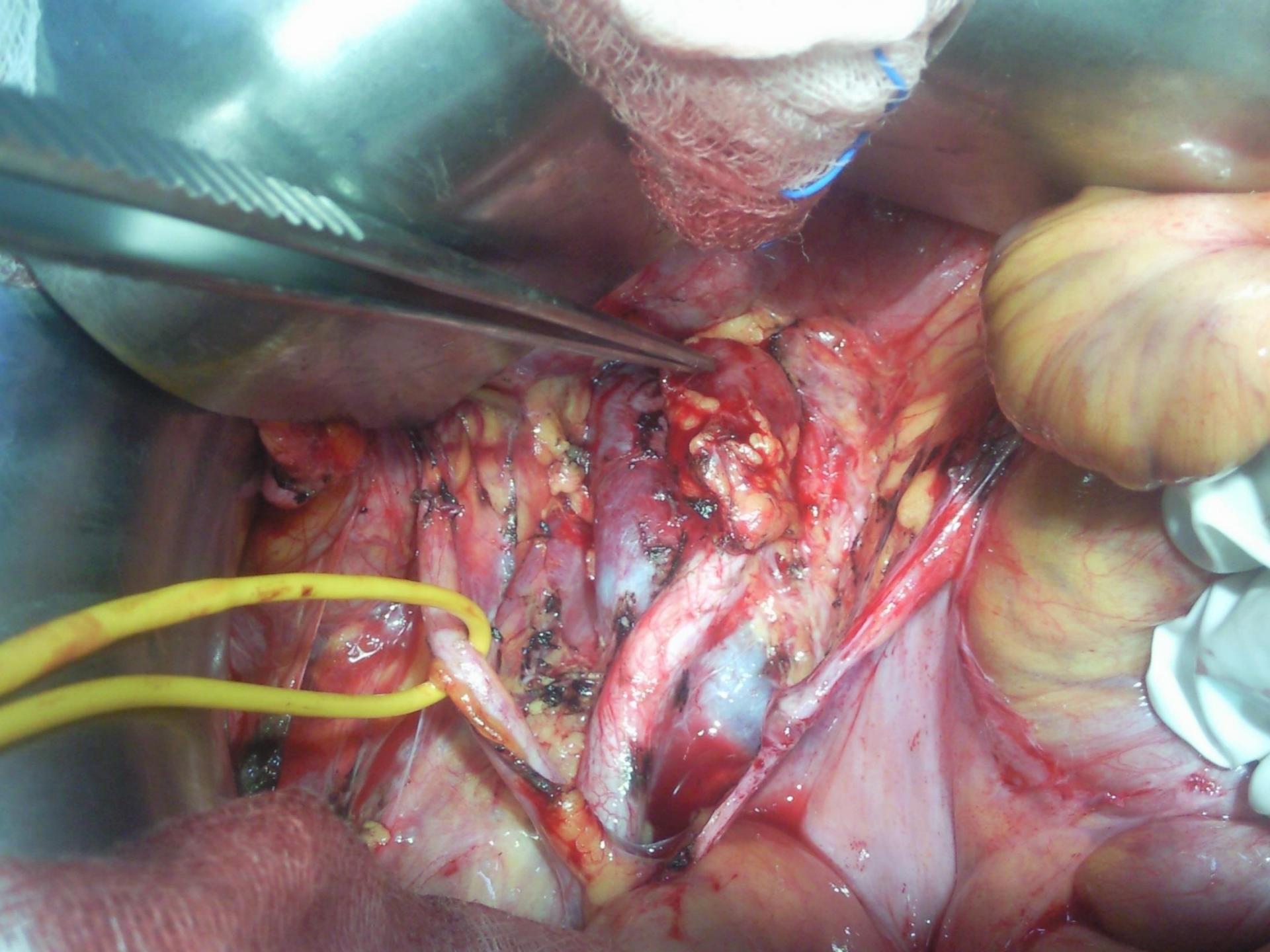
## Effect of Incorporation of Bevacizumab on Survival.

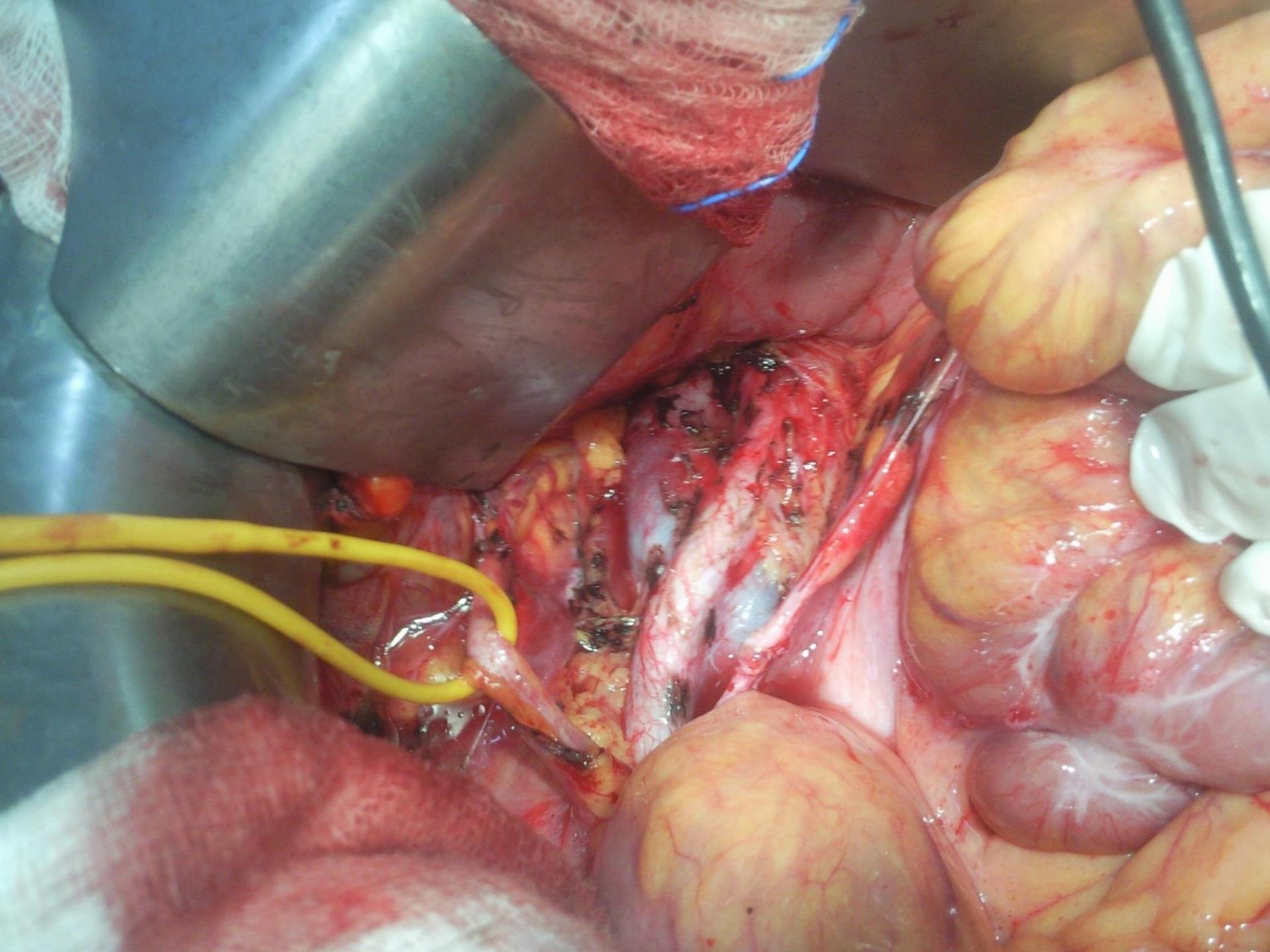


Tewari KS et al. N Engl J Med 2014;370:734-743



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# Cervical cancer prevention

Sexual education

HPV-vaccination

Liquid-based cytology sampling

HPV-based screening





## Globocan 2020

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# Corpus cancer pathogenesis

Unopposed estrogen exposure  
Insulin-resistance  
Extragonadal aromatase activity  
POLE  
MSI-h  
P53, p21 mutations



# Prognostic factors in corpus cancer

- TNM and FIGO stages, tumor-size, cervical spread, adnexal spread, lymphatic spread
- Histological type, grade
- Depth of myometrial invasion
- LVSI
- Distant spread



# Corpus cancer clinical and radiological work-up

- Pelvic examination and endometrial biopsy
- Pelvic MRI
- Vaginal  $\pm$  rectal US
- Chest and abdominal CT or whole body PET-CT
- Cystoscopy or rectoscopy if bladder or rectum suspicious for spread

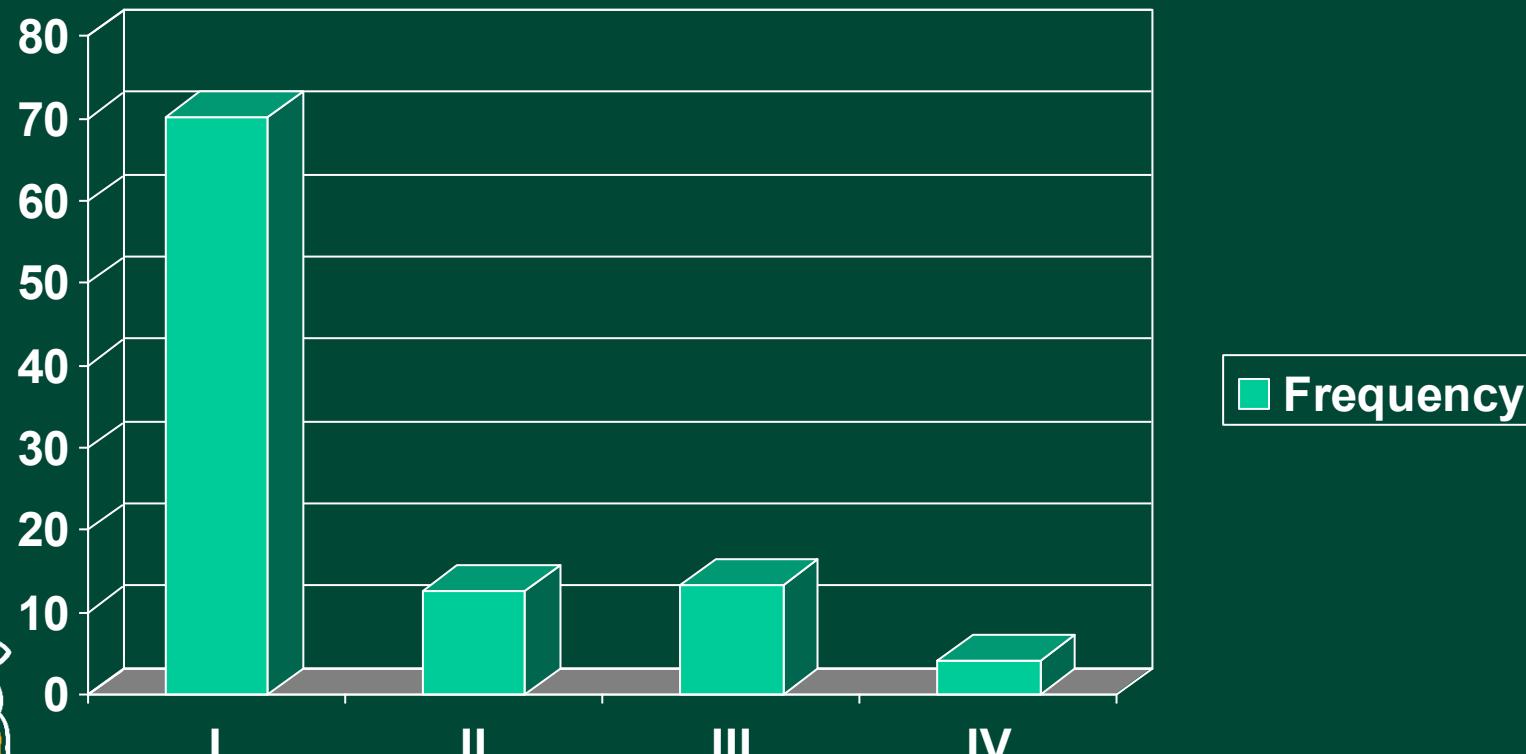


# Corpus cancer - Origin

- Endometrial cancer
  - Endometrial stroma sarcoma
  - Myometrial sarcoma

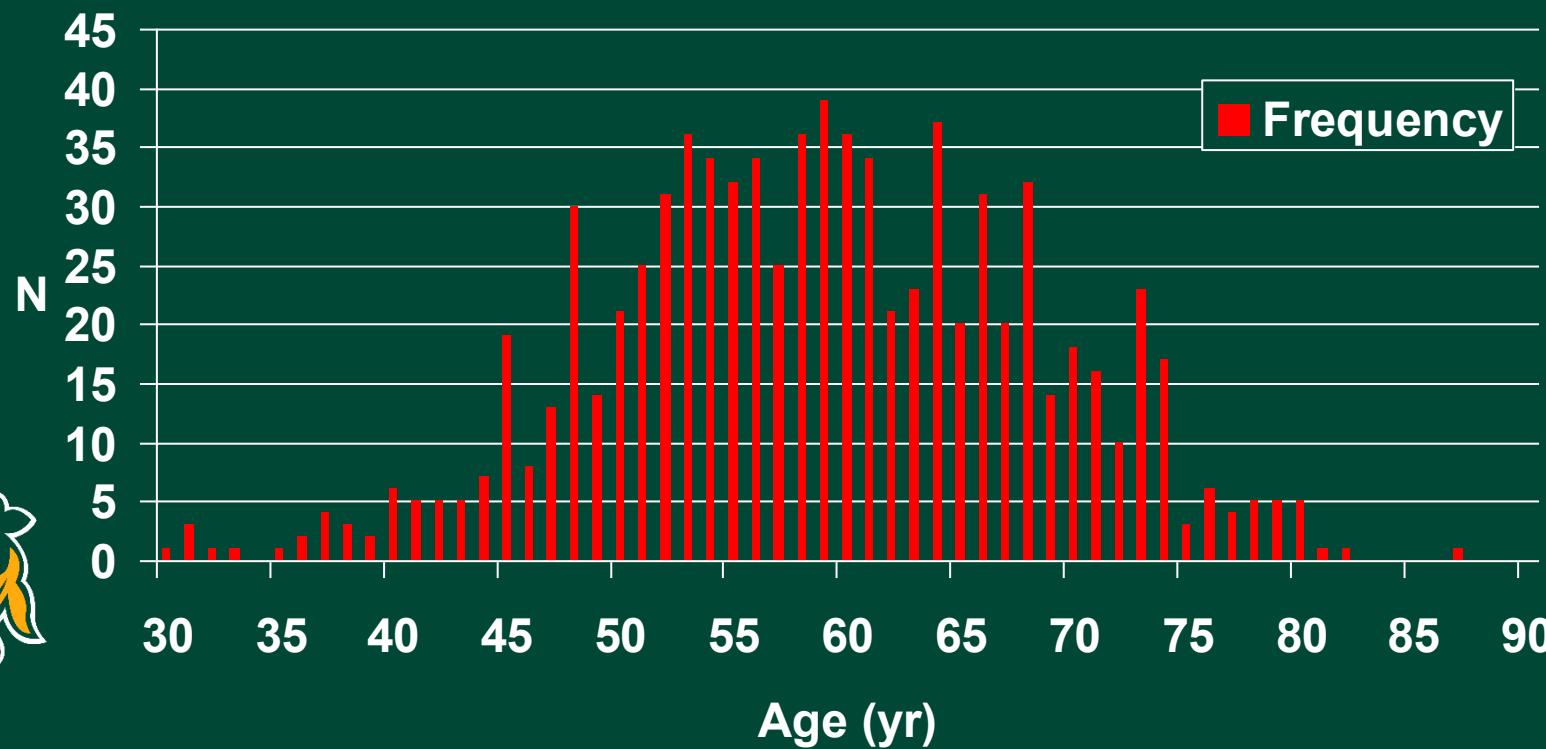


# Endometrial cancer stage-distribution (%)



# Age distribution in endometrial cancer

N=817

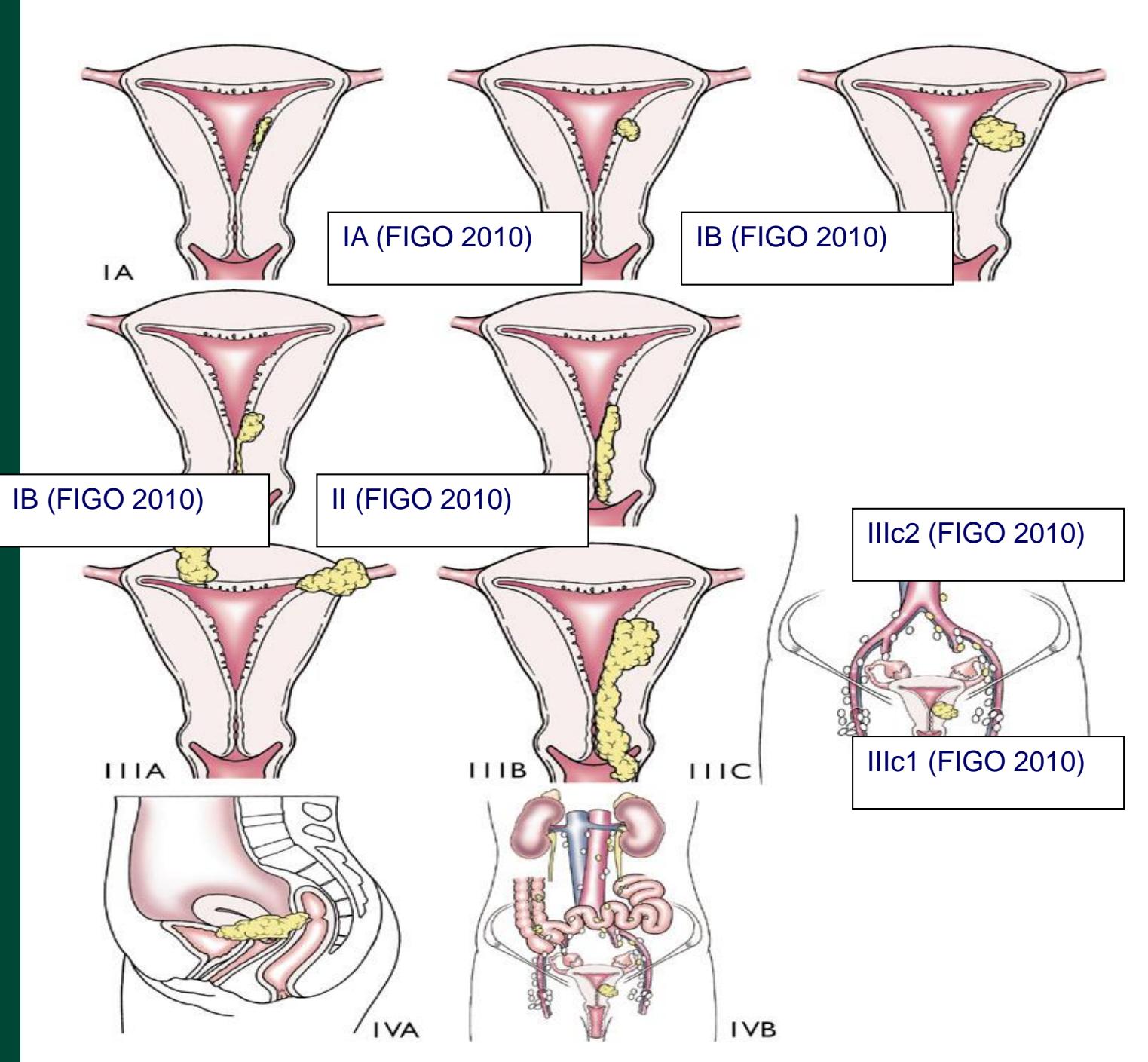


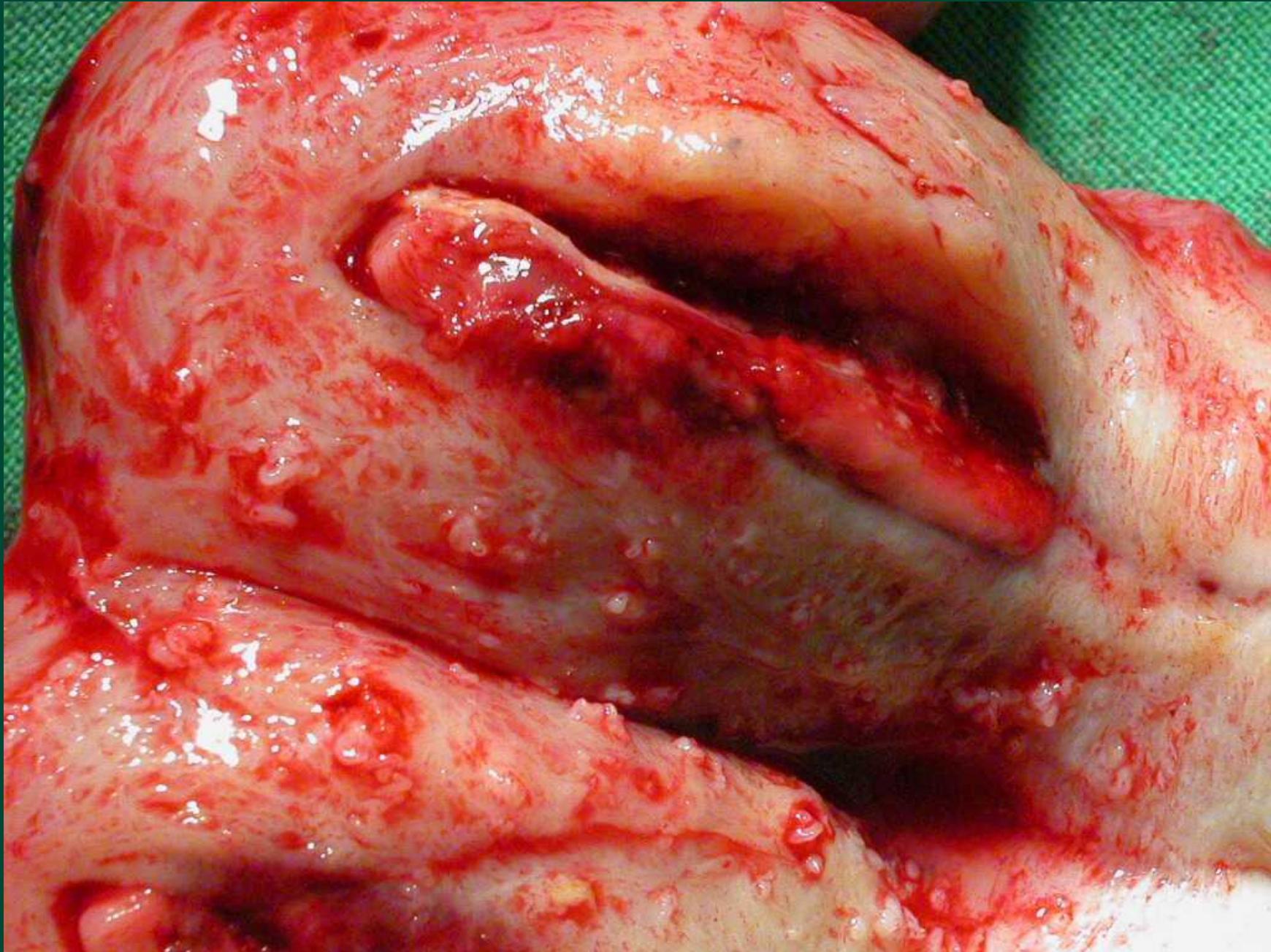
# Gynecologic tumors

## Staging in general

- I      localized to organ of origin
- II     spread to adjacent tissues
- III    regional lymphatic spread
- IV    distant metastasis







# Corpus cancer treatment

- Surgery (TAH+BSO $\pm$ lymphadenect)
- Radiotherapy (adjuvant or primary)
- Chemotherapy (adjuvant or primary)
- Gestogen therapy (adjuvant)
- Aromatase inhibitors
- Investigational therapies (TKI, CHKI, PARPi)



# Five-year survival

Surgery	84%
Radiotherapy	45,3%
Radiosurgery	83,6%
Surgery+Radiotherapy	82,4%
Surgery+Chemotherapy	59,8%
Hormonal therapy	42,9%



# Corpus cancer prevention

- Combined oral contraceptives >10yrs
- Bodyweight control
- Oncological surveillance, TVUS screening
- Progestogenic opposition





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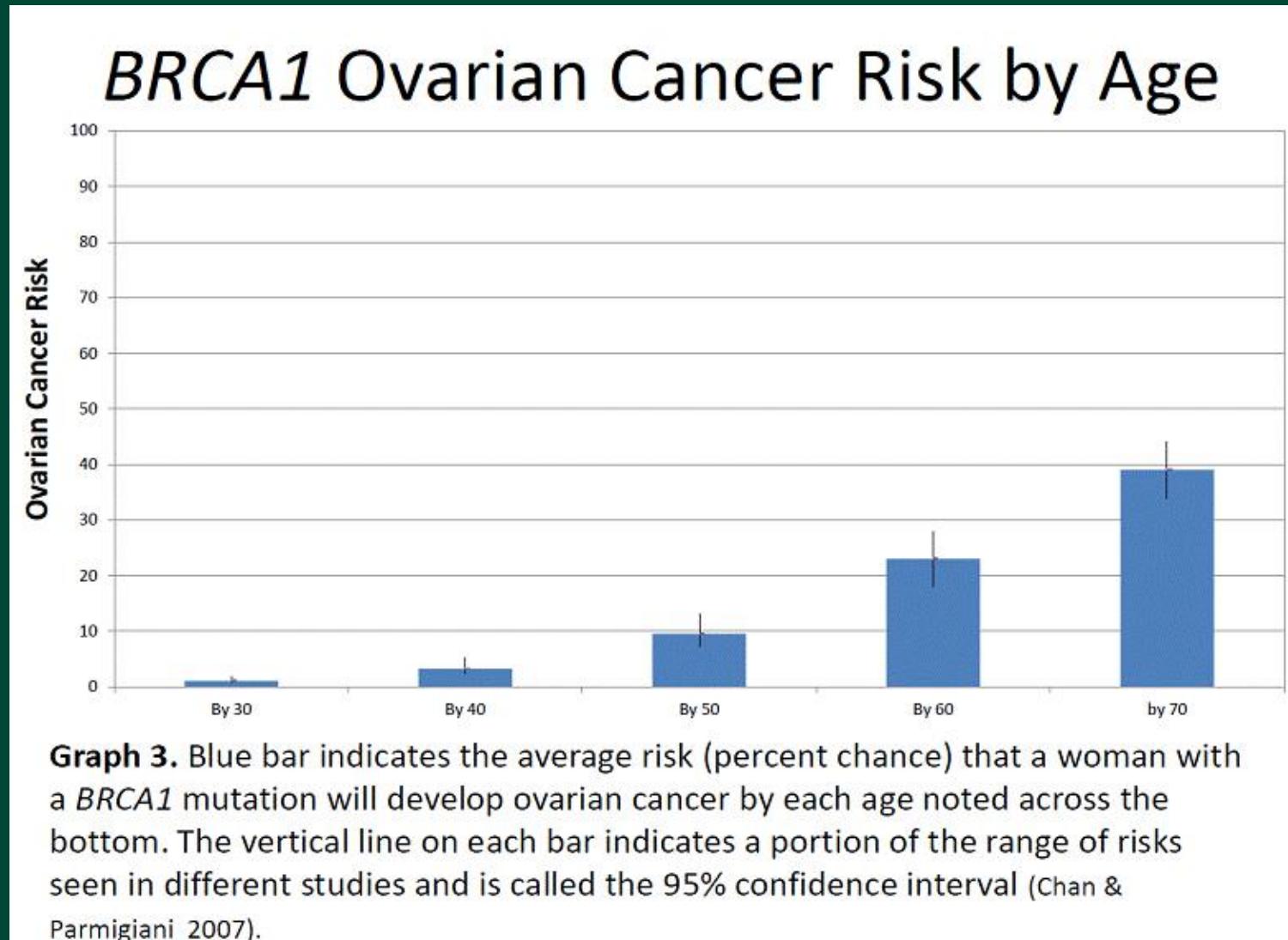
# Ovarian cancer - Origin

- Epithelial
  - Sexcord-stromal
  - Germ cell



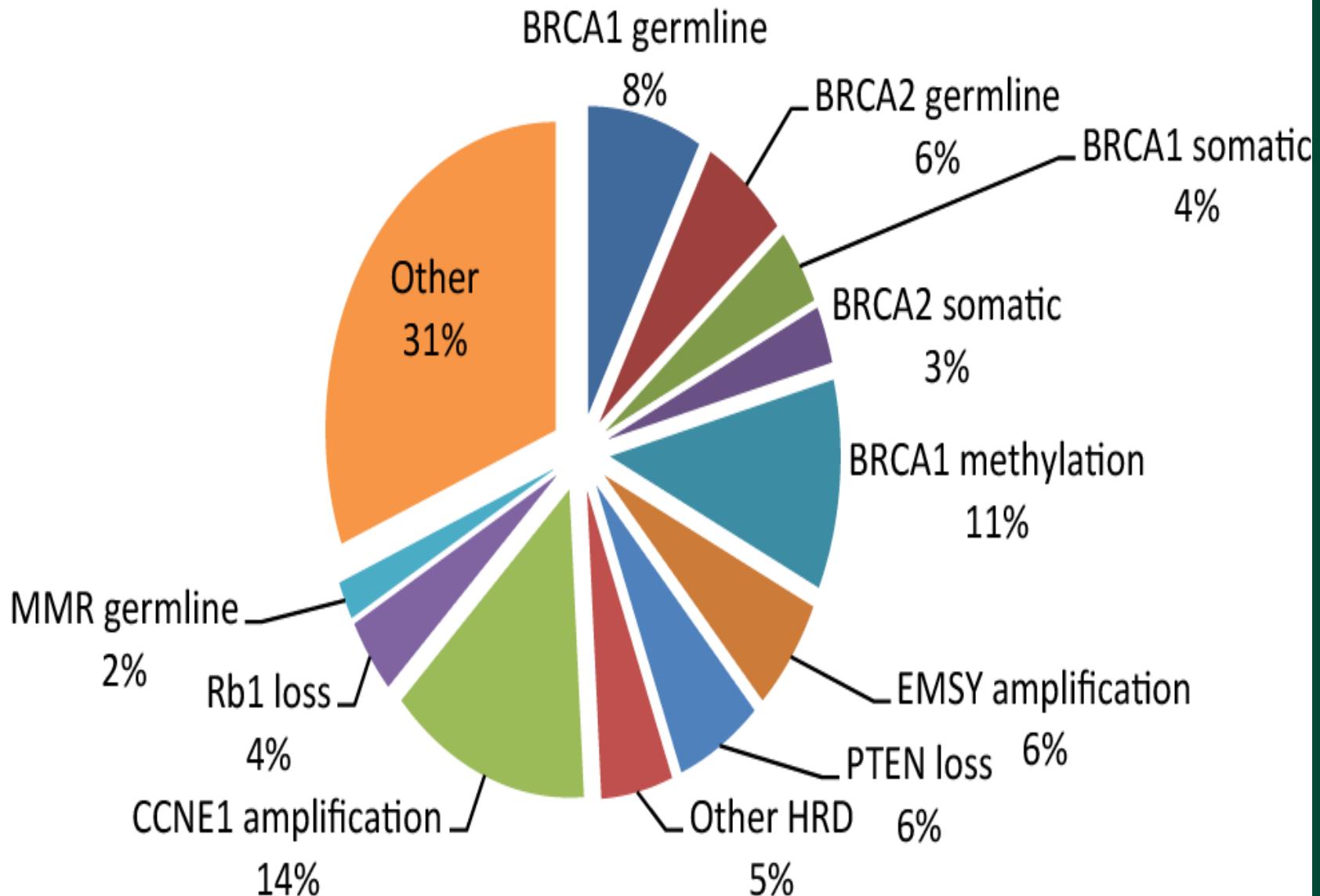


# Ovarian cancer - Pathogenesis

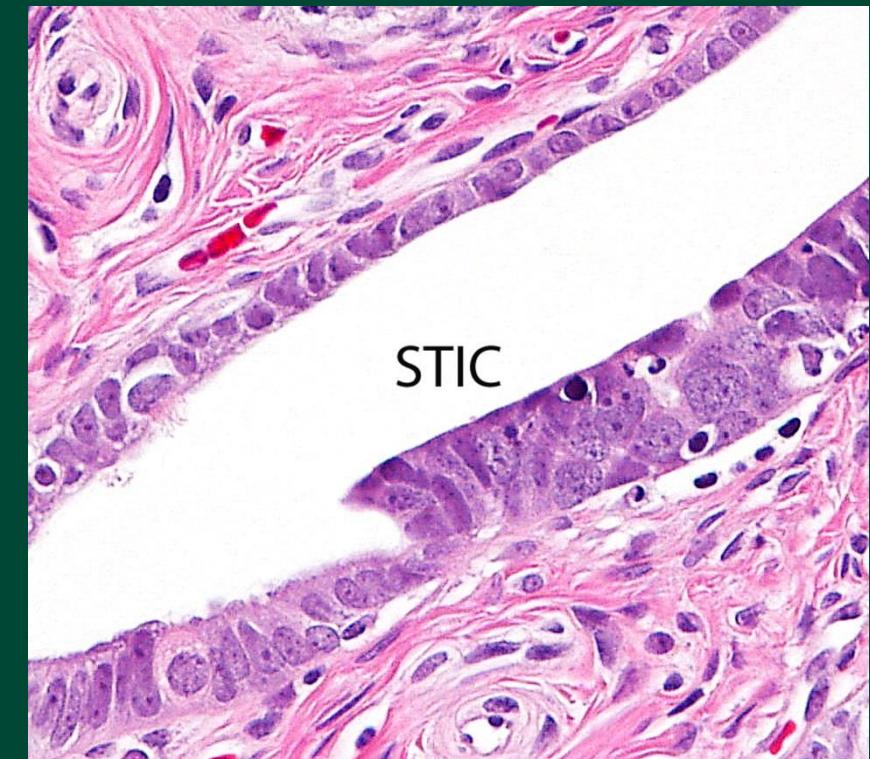
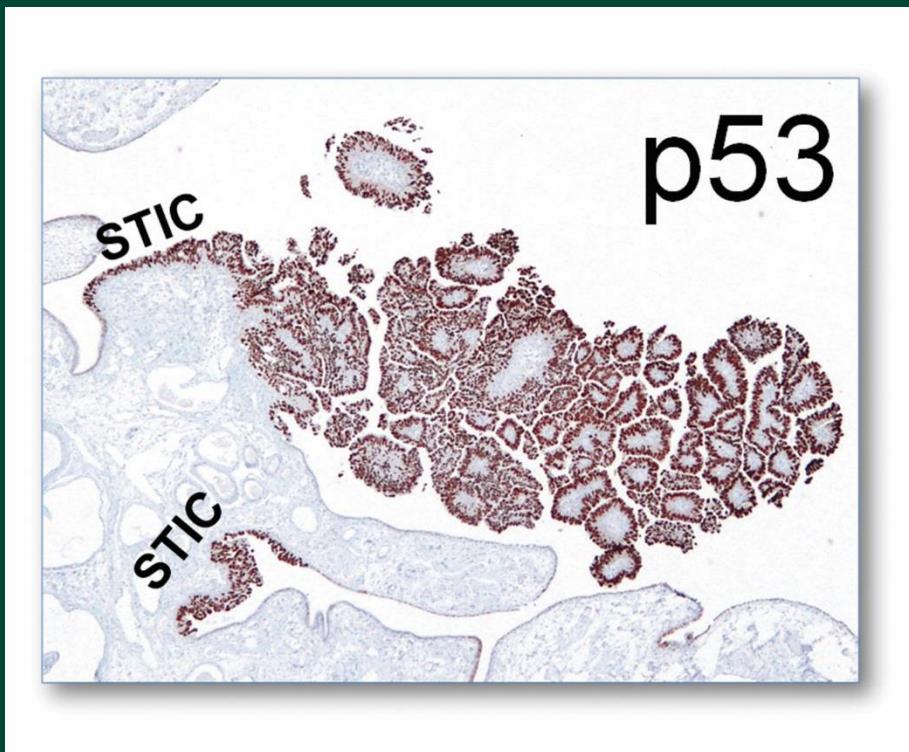




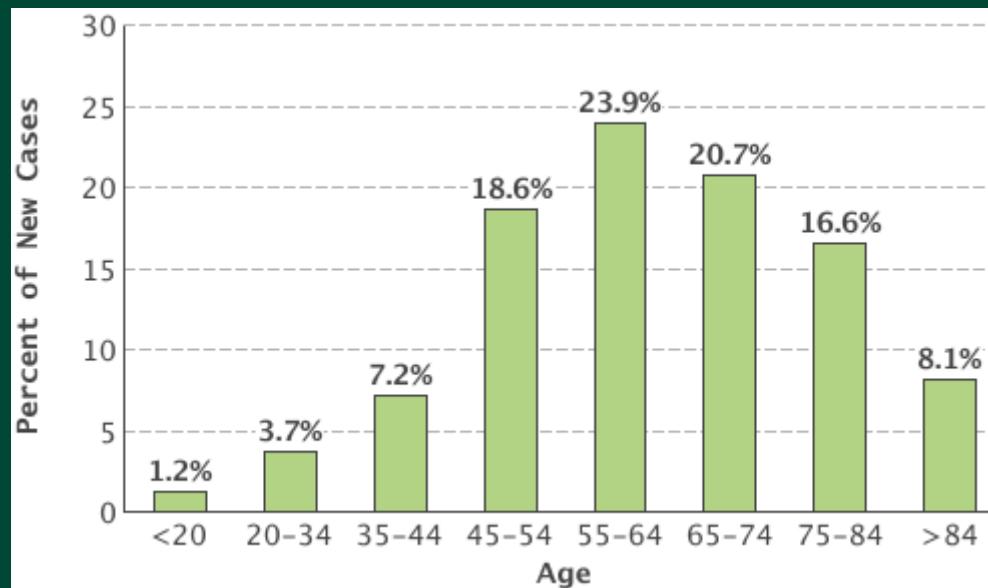
# Molecular Profiling of Serous Ovarian Cancer



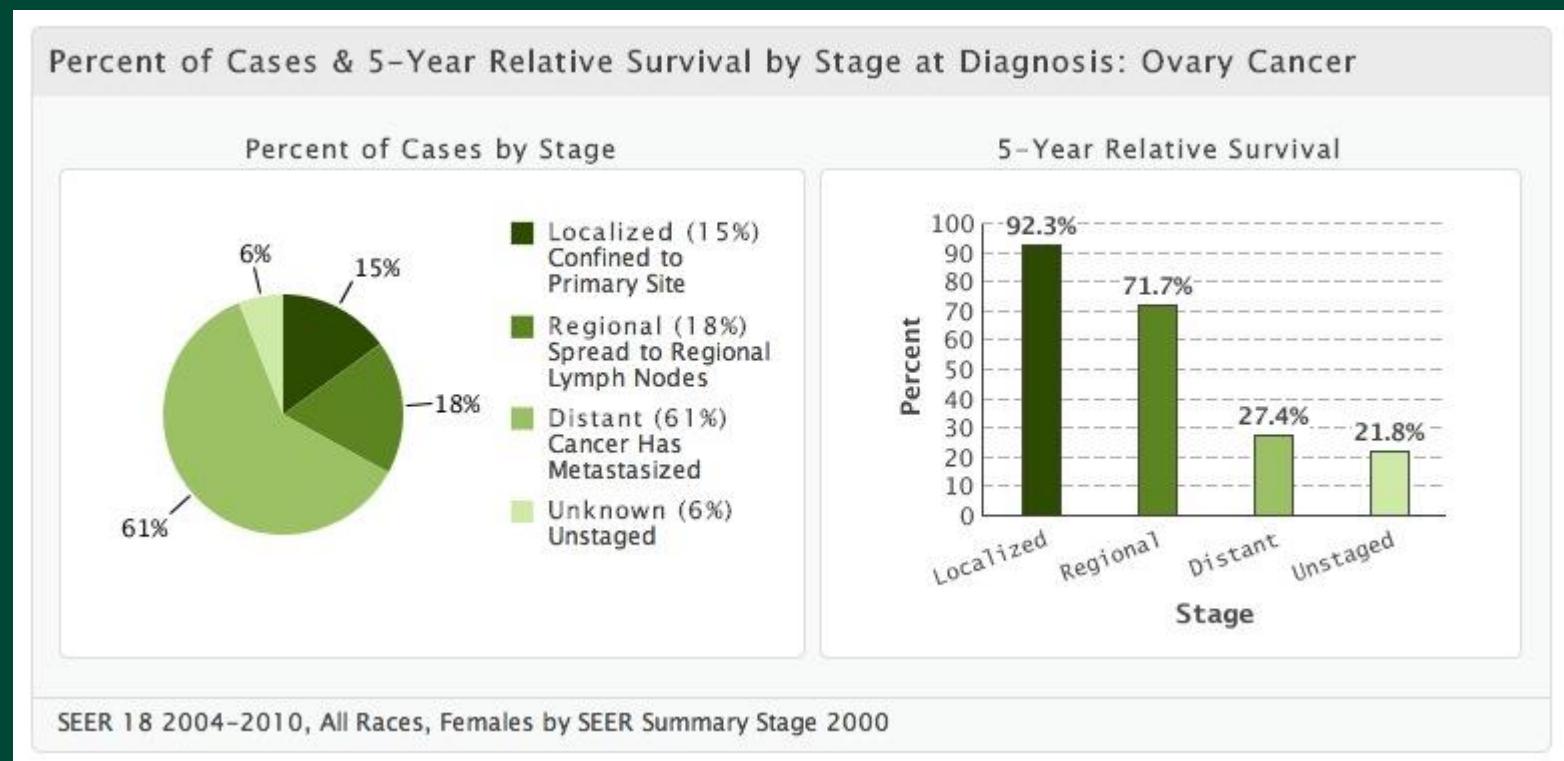
# Ovarian cancer - Pathogenesis



# Ovarian cancer - Age distribution



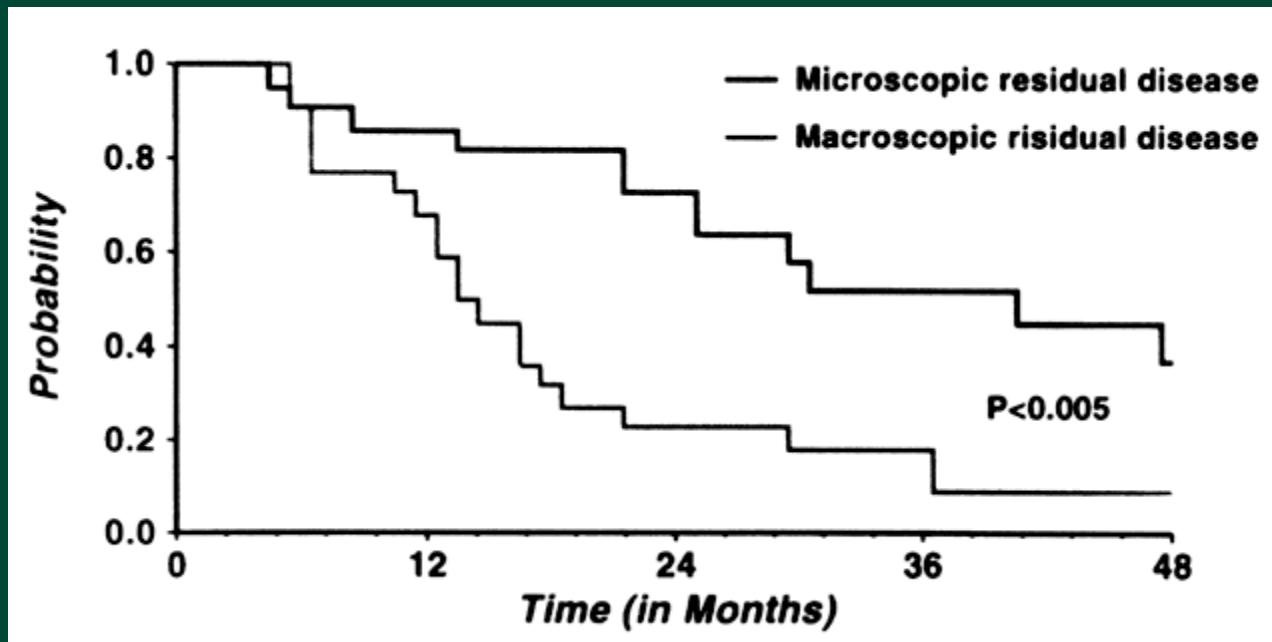
# Ovarian cancer – Stage distribution







# Role of debulking surgery in ovarian cancer



# Ovarian cancer staging refined in 2014

- Ic replaced by Ic1 (surgical rupture), Ic2 (presurgical rupture), Ic3 (pos.perit.cytol.)
- IIc discarded
- IIIa replaced by IIIa1 (pos.node, <10mm IIIa1i, >10mm IIIa1ii) and IIIa2 (microscopic omental metastasis)
- IV replaced by IVa (hydrothorax pos.cytol.) and IVb (parenchymal liver met or other distant met)



Ovarian cancer stages  
are not phases of a continuity,  
but merely a description of the extent of disease

- Ia, Ib, Ic1, Ic2, Ic3
- IIa, IIb
- IIIa1i, IIIa1ii, IIIa2, IIIb, IIIc
- IVa, IVb



# FIRST-LINE THERAPY – Standard Treatment Options



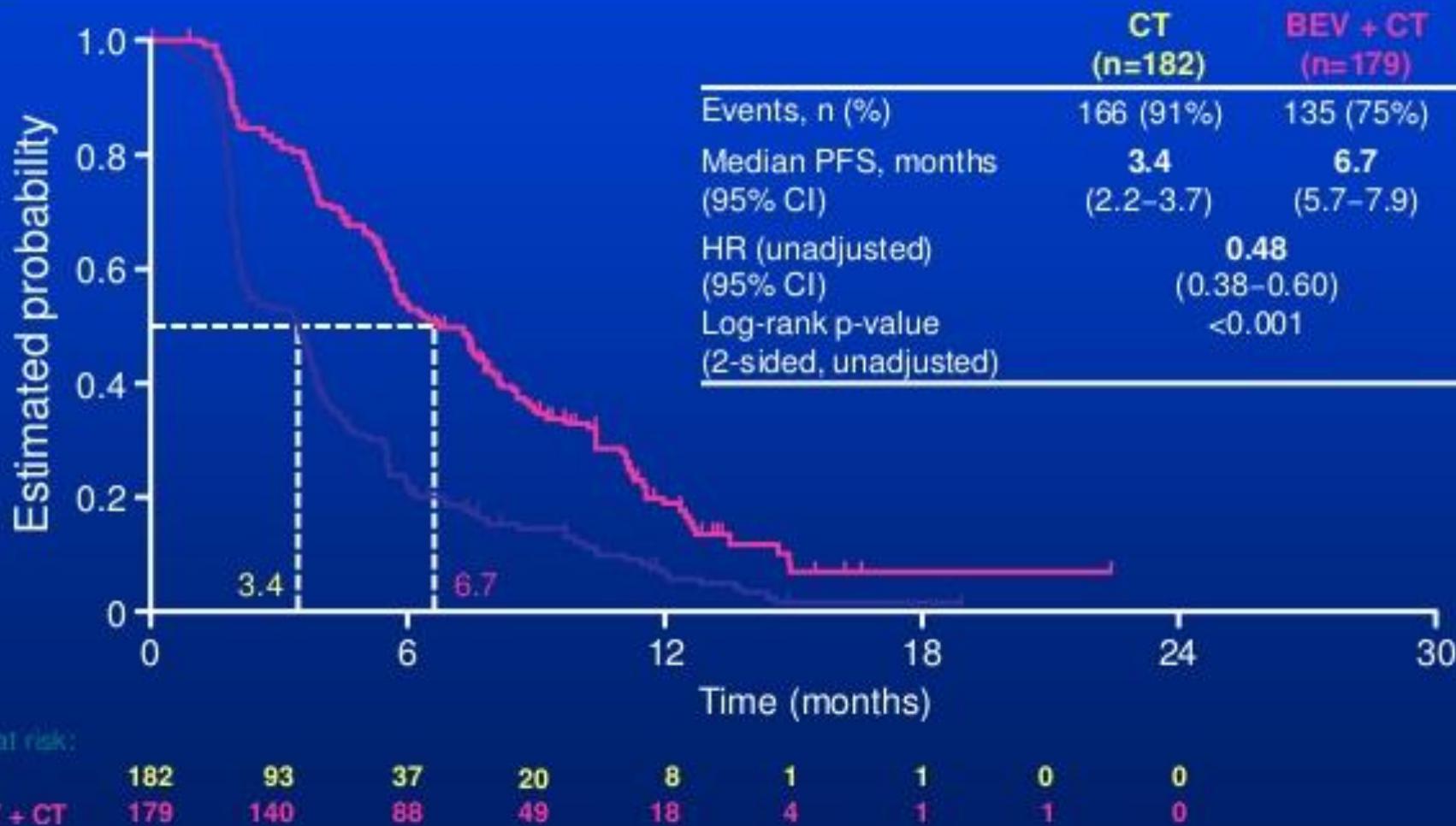
Surgery with maximum  
cytoreduction effort <1cm  
residual disease



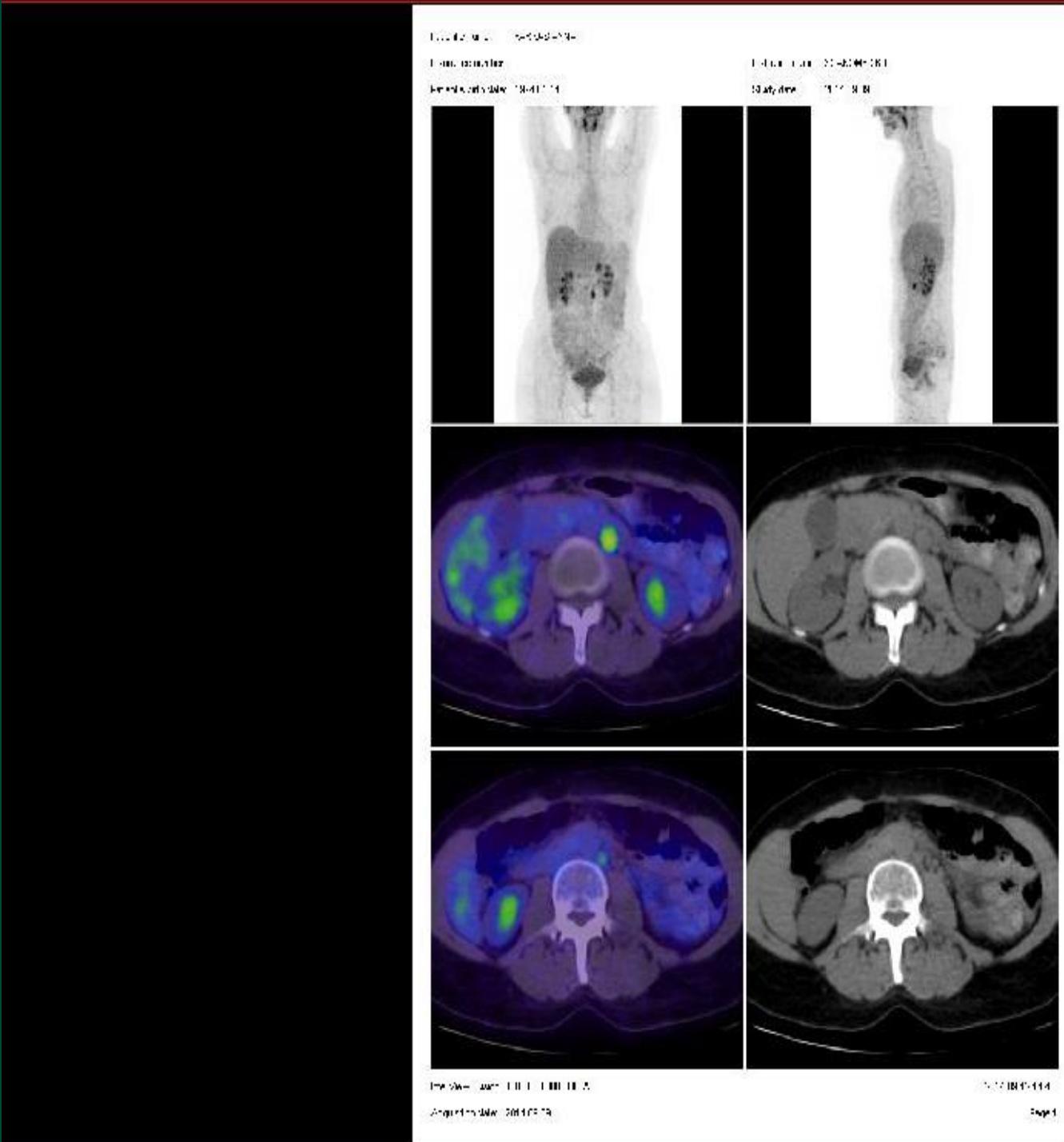
Platinum + Taxane Chemotherapy  
(Carboplatin + Paclitaxel)



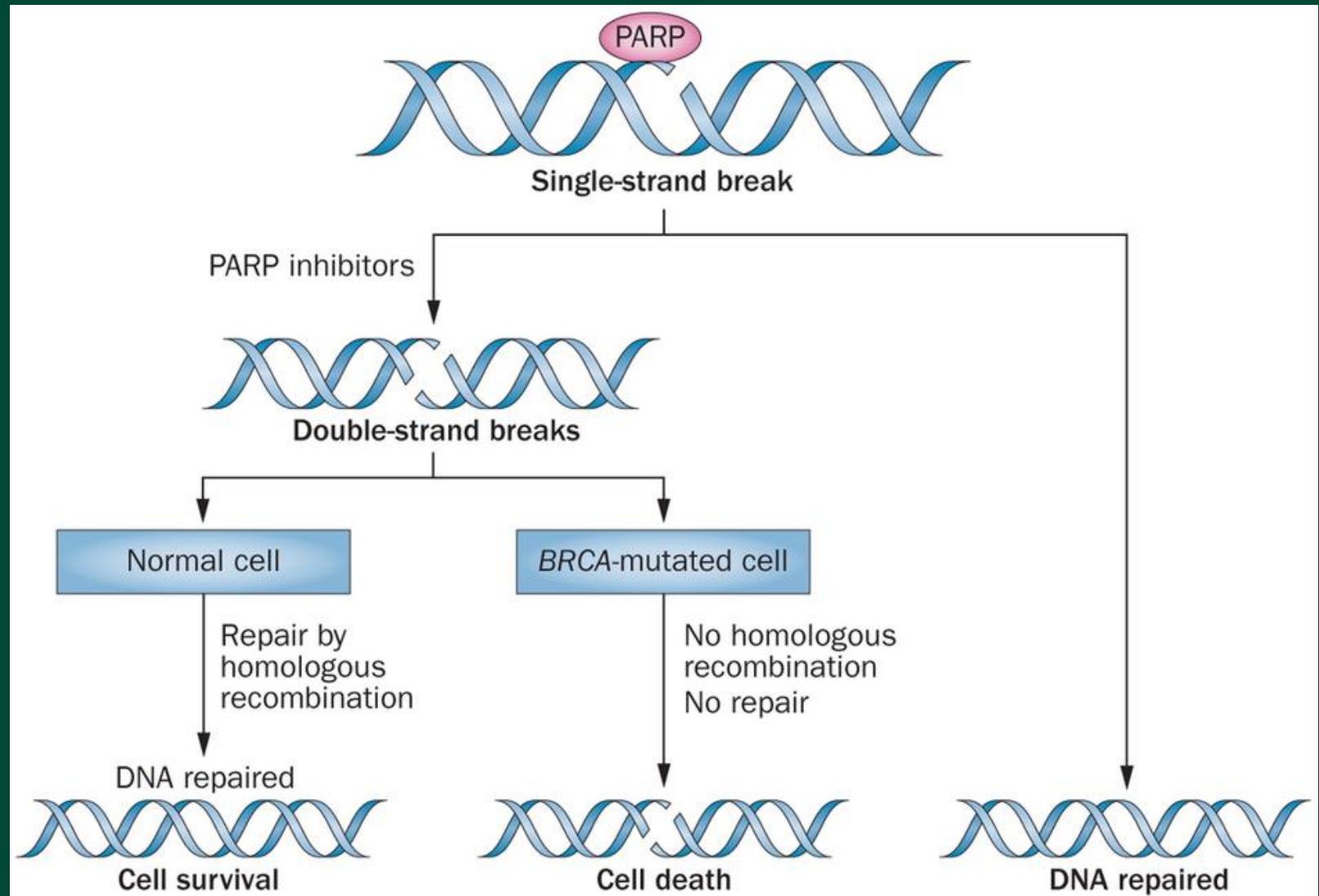
# Aurelia: Platinum Resistant PFS



Pujade Luraine et al. JCO 30:LBA 5002, 2012



# Synthetic lethality



# Key points summary of ovarian cancer treatment

- Primary treatment of ovarian cancer is surgical debulking aiming at maximal cytoreduction.
- Best prognostic indicator is the quality of primary surgery and the amount of residual disease (*IIa level evidence, Type B recommendation*).
- Surgical treatment should be performed in centers with experience and infrastructure for radical resection (e.g. bowel surgery) (*III. level evidence, Type B recommendation*).
- Success of cytoreductive surgery is largely dependent on the experience, skill and determination of the surgeon (*1B level evidence*).
- Adjuvant chemotherapy (taxol; carboplatin; pegilated liposomal doxorubicin; topotecan; gemcitabine) prolongs progression-free and overall survival.
- Future directions of adjuvant treatment: neoangiogenesis inhibitors, PARP inhibitors, checkpoint inhibitors



# Ovarian cancer prevention

- Combined oral contraceptives >10yrs
- Tamoxifen
- Oncological surveillance, screening  
(TVUS, CA125, ROMA-score)
- Prophylactic salpingectomy, salpingo-oophorectomy in high-risk population



# **Thank you for your attention!**

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[www.drpokarobert.com](http://www.drpokarobert.com)

