

# Il tumore della cervice uterina

## Trattamento Conservativo



**MUGO4**  
MILAN ULTRASOUND  
GYNECOLOGIC ONCOLOGY



Dorella Franchi  
Preventive Gynecologic Unit  
European Institute of Oncology

# Cervical cancer

## Epidemiology

- Fourth most frequent cancer in women
- 570,000 new cases in 2018 (6.6% of all female cancers)
- 311.000 deaths in 2018 (approximately 90% occurred in low- and middle-income countries)
- Virtually all cervical cancers are associated with human papilloma viruses (HPV)



# Cervical Cancer - Hystology

Squamous Cancer

80%

Adenocarcinoma

15%

Usual Type

Adenosquamous

Adenomucinous

SMILE

HPV related

Endometrioid AdenoCa

Mucinous Gastric Type

Malignant Adenoma

Clear Cell

Mesonephric Type

Neuroendocrin Type

Undifferentiated Carcinoma

5%

NON HPV related

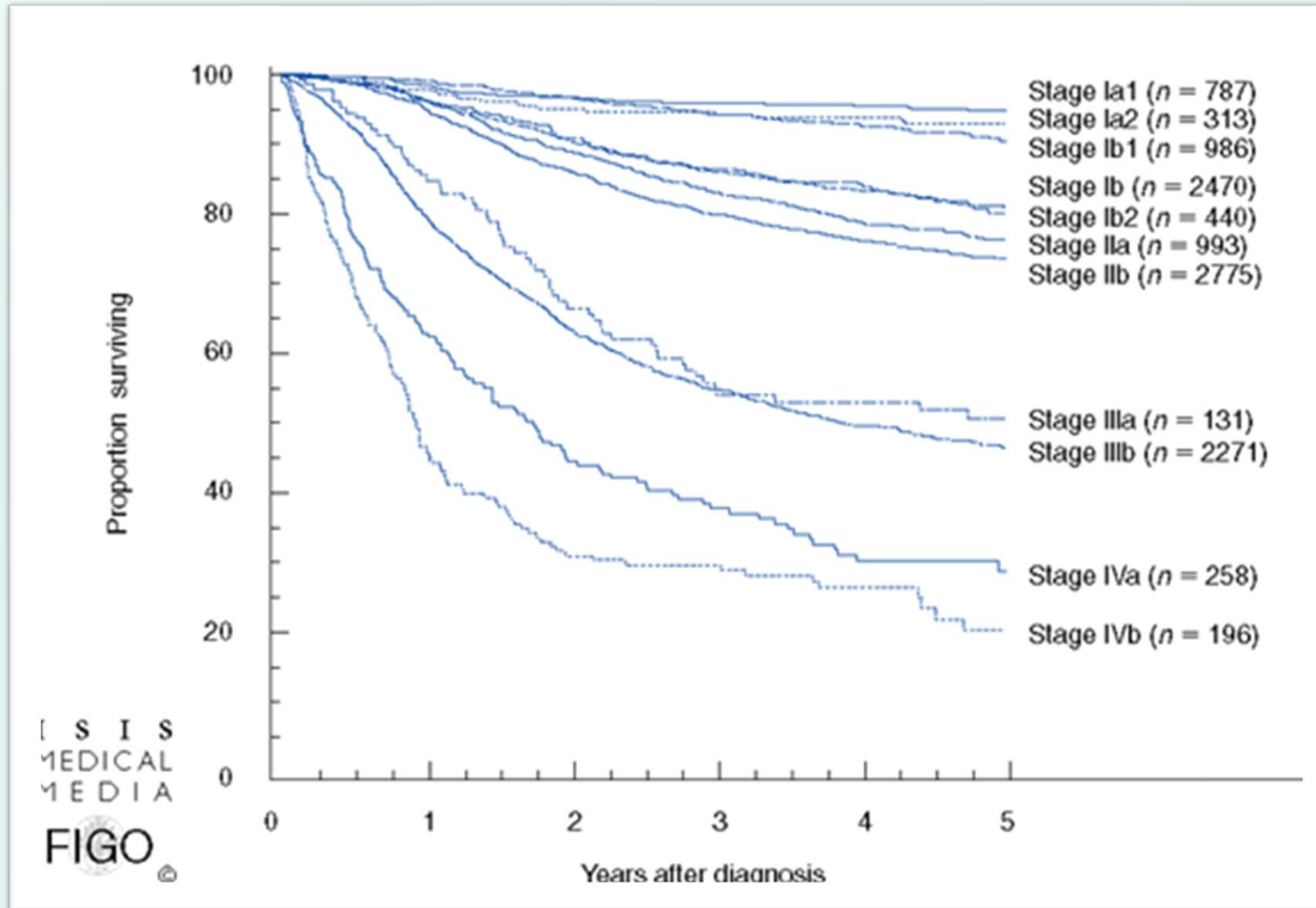
# Cervical cancer

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## Prognostic factors

- TNM and FIGO stage (including tumor size extracervical tumor extension and nodal involvement)
- Depth of cervical stromal invasion and a minimum thickness of uninvolved cervical stroma
- Lymphovascular space involvement (LVSI)
- Distant metastasis

# Survival by stage



## Revised FIGO staging for carcinoma of the cervix uteri<sup>☆</sup>

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Seija Grenman<sup>5</sup> | Kanishka Karunaratne<sup>6</sup> | Sean T. Kehoe<sup>7</sup> | Ikuo Konishi<sup>8</sup> |  
Alexander B. Olawaiye<sup>9</sup> | Jaime Prat<sup>10</sup> | Rengaswamy Sankaranarayanan<sup>11,12</sup>

### Box 1 FIGO staging of carcinoma of the cervix uteri (2018).

#### Stage I:

The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded)

- **IA** Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5 mm<sup>a</sup>
  - **IA1** Measured stromal invasion <3 mm in depth
  - **IA2** Measured stromal invasion ≥3 mm and <5 mm in depth
- **IB** Invasive carcinoma with measured deepest invasion ≥5 mm (greater than stage IA), lesion limited to the cervix uteri<sup>b</sup>
  - **IB1** Invasive carcinoma ≥5 mm depth of stromal invasion and <2 cm in greatest dimension
  - **IB2** Invasive carcinoma ≥2 cm and <4 cm in greatest dimension
  - **IB3** Invasive carcinoma ≥4 cm in greatest dimension

#### Stage II:

The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall

- **IIA** Involvement limited to the upper two-thirds of the vagina without parametrial involvement
  - **IIA1** Invasive carcinoma <4 cm in greatest dimension
  - **IIA2** Invasive carcinoma ≥4 cm in greatest dimension
- **IIB** With parametrial involvement but not up to the pelvic wall

#### Stage III:

The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes<sup>c</sup>

- **IIIA** Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
- **IIIB** Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- **IIIC** Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)<sup>c</sup>
  - **IIIC1** Pelvic lymph node metastasis only
  - **IIIC2** Paraaortic lymph node metastasis

#### Stage IV:

The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV

- **IVA** Spread of the growth to adjacent organs
- **IVB** Spread to distant organs

- ✓ Stage IA : only infiltration depth!
- ✓ Stage IB : substaged in B1-2-3
- ✓ Stage IIIC: substaged according to N + ( pelvic or paraaortic)

From Clinical staging - - >  
To Clinical, radiological and surgical staging

# Cervical Cancer – standard management

## Stage IA – IB2

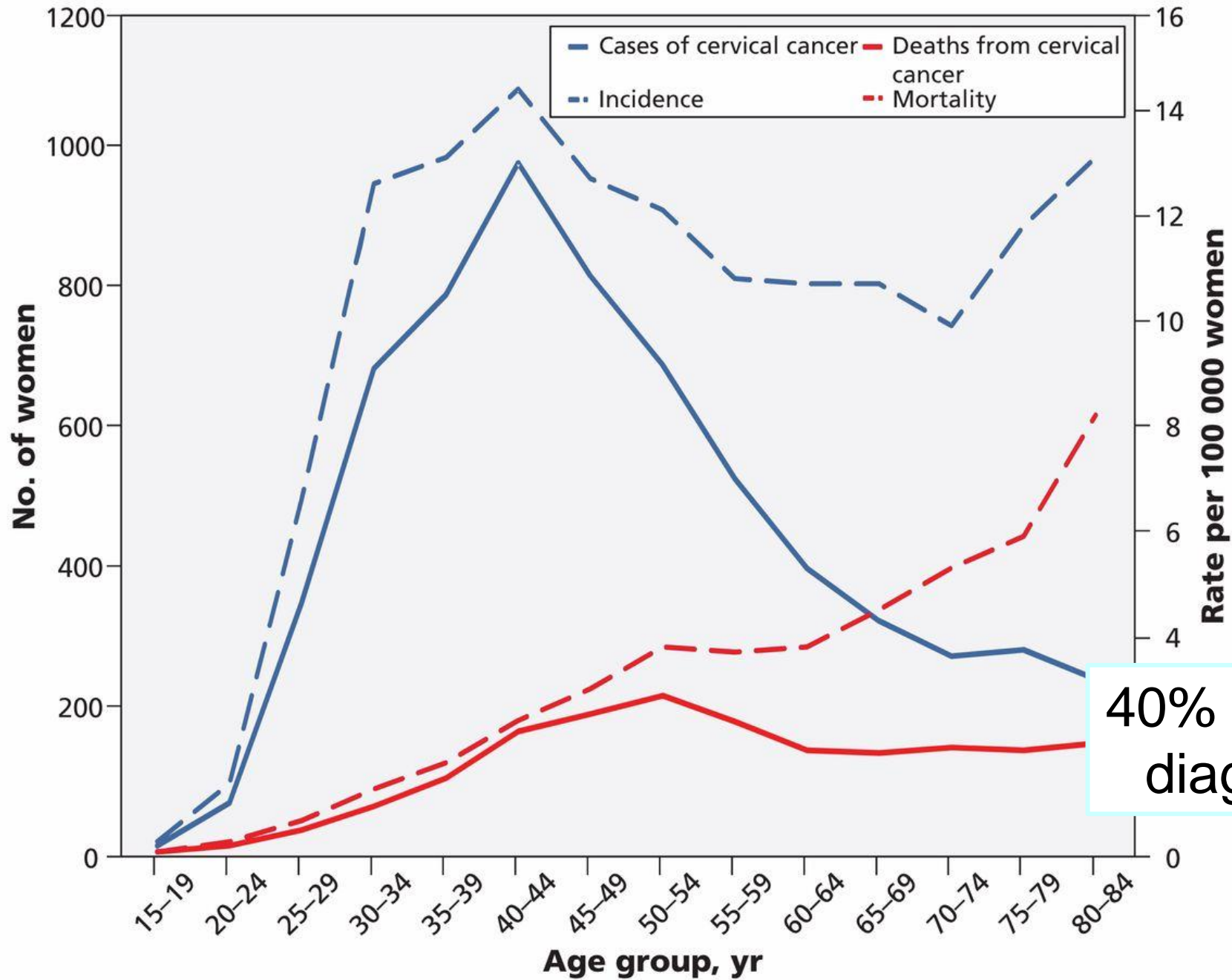
- Tumors < 4 cm with no parametrial invasion)
- **Radical hysterectomy + lymphadenectomy (except stage IA1)**

## Stage $\geq$ IB3

- Tumors > 4 cm or parametrial invasion) or bulky lymphnodes
- **Radiotherapy/Chemiotherapy or NACHT+ Surgery**

## Exception

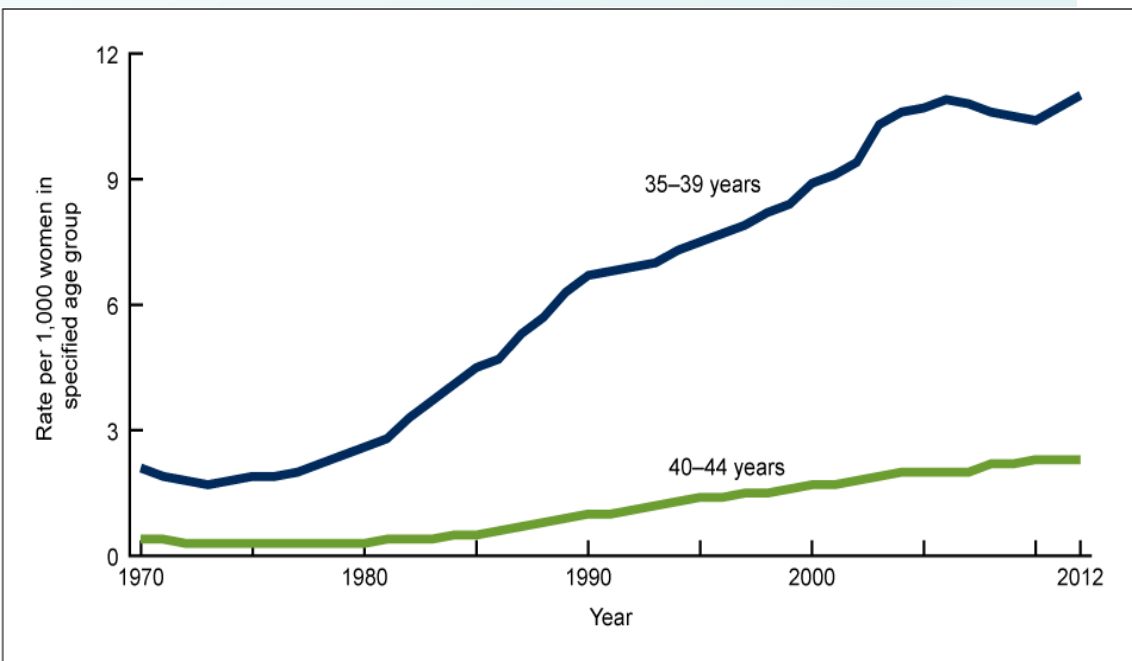
- exophytic tumors > 4 cm, with no parametrial engagement -> **surgery**



40% of cervical cancer are diagnosed in fertile age



## First birth rate by selected age of mother



NOTE: Access data table for Figure 1 at: [http://www.odc.gov/nchs/data/databriefs/db152\\_table.pdf#1](http://www.odc.gov/nchs/data/databriefs/db152_table.pdf#1).  
SOURCE: CDC/NCHS, National Vital Statistics System.



# Fertility Sparing Treatment



- ✓ Fertility preservation
- ✓ Oncological outcome



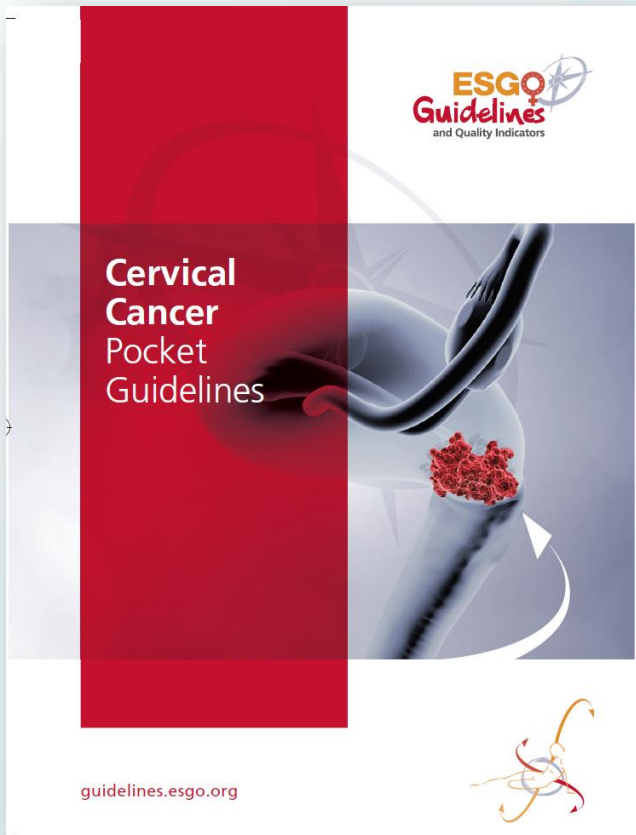
The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer

David Cibula <sup>a,\*</sup>, Richard Pötter <sup>b</sup>, François Planchamp <sup>c</sup>, Elisabeth Avall-Lundqvist <sup>d</sup>, Daniela Fischerova <sup>a</sup>, Christine Haie Meder <sup>e</sup>, Christhardt Köhler <sup>f</sup>, Fabio Landoni <sup>g</sup>, Sigurd Lax <sup>h</sup>, Jacob Christian Lindegaard <sup>i</sup>, Umesh Mahantshetty <sup>j</sup>, Patrice Mathevet <sup>k</sup>, W. Glenn McCluggage <sup>l</sup>, Mary McCormack <sup>m</sup>, Raj Naik <sup>n</sup>, Remi Nout <sup>o</sup>, Sandro Pignata <sup>p</sup>, Jordi Ponce <sup>q</sup>, Denis Querleu <sup>c</sup>, Francesco Raspagliesi <sup>r</sup>, Alexandros Rodolakis <sup>s</sup>, Karl Tamussino <sup>t</sup>, Pauline Wimberger <sup>u</sup>, Maria Rosaria Raspollini <sup>v</sup>

## Fertility Sparing Treatment (FST)

- ✓ Before starting FST, consultation at a fertility center is recommended.
- ✓ FST only in gynecologic-oncological centers (expertise in this kind of oncologic therapy).
- ✓ Prognostic factors, clinical staging, and preoperative workup do not differ from those who do not consider FST.
- ✓ Squamous cell carcinoma or usual-type (HPV-related) adenocarcinoma  $\leq 2$  cm of the largest diameter
- ✓ FST not recommended for rare histological subtypes (more aggressive behavior).
- ✓ FST abandonment if : lymph node involvement or positive margins

# Diagnostic preoperative work-up



## Local clinical and radiological diagnostic work-up

- ✓ Pelvic examination and biopsy +/- colposcopy are mandatory components to diagnose cervical cancer.
- B** Pandatory initial work-up for assessment of pelvic tumour extent and to guide treatment options is pelvic magnetic resonance imaging (MRI).
- ✓ Endovaginal/transrectal ultrasound is an option if performed by a properly trained sonographer.

- B** In locally advanced cervical cancer (T1b2 and higher (except T2a1) or in early stage disease with suspicious lymph nodes on imaging, positron emission tomography-computed tomography (PET-CT) or chest/abdomen computed tomography (CT) is recommended for assessment of nodal and distant disease.

# Can TVUS be used to guide the management of cervical cancer in young patients ?



2008

### Transrectal ultrasound and magnetic resonance imaging in staging of early cervical cancer

D. FISCHEROVA\*, D. CIBULA\*, H. STENHOVA†, H. VONDRICHOVA†, P. CALDA\*, M. ZIKAN\*, P. FREITAG\*, J. SLAMA\*, P. DUNDR‡ & J. BELACEK§

\*Oncogynecological Center, Department of Obstetrics and Gynecology, General Teaching Hospital, Charles University, Prague, Czech Republic; †Diagnostic Center Mediscan, Prague, Czech Republic; ‡Department of Pathology, General Teaching Hospital, Charles University, Prague, Czech Republic; and §Institute of Biophysics and Informatics, First Medical School, Charles University, Prague, Czech Republic

In a series of 95 cases

TRU > MRI to detect small cervical cancers (<1 cm)

TRU more sensitive than MRI for detecting parametrial involvement (83 % vs 50 %)

2009

### Transvaginal ultrasonography and magnetic resonance imaging for assessment of presence, size and extent of invasive cervical cancer

A. C. TESTA\*, M. LUDOVISI†, R. MANFREDI‡, G. ZANNONI§, B. GUI¶, D. BASSO\*, A. DI LEGGE\*, A. LICAMELI\*, R. DI BIDINO\*\*, G. SCAMBIA\* and G. FERRANDINA\*†

68 women with cervical cancer

TVS = MRI tumor detection and tumor size

TVS more sensitive than MRI for identifying parametrial involvement (60 % vs 40 %). p=ns



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Contents lists available at SciVerse ScienceDirect

Gynecologic Oncology

2014

journal homepage: www.elsevier.com/locate/ygyno



### Early-stage cervical cancer: Tumor delineation by magnetic resonance imaging and ultrasound – A European multicenter trial☆☆☆

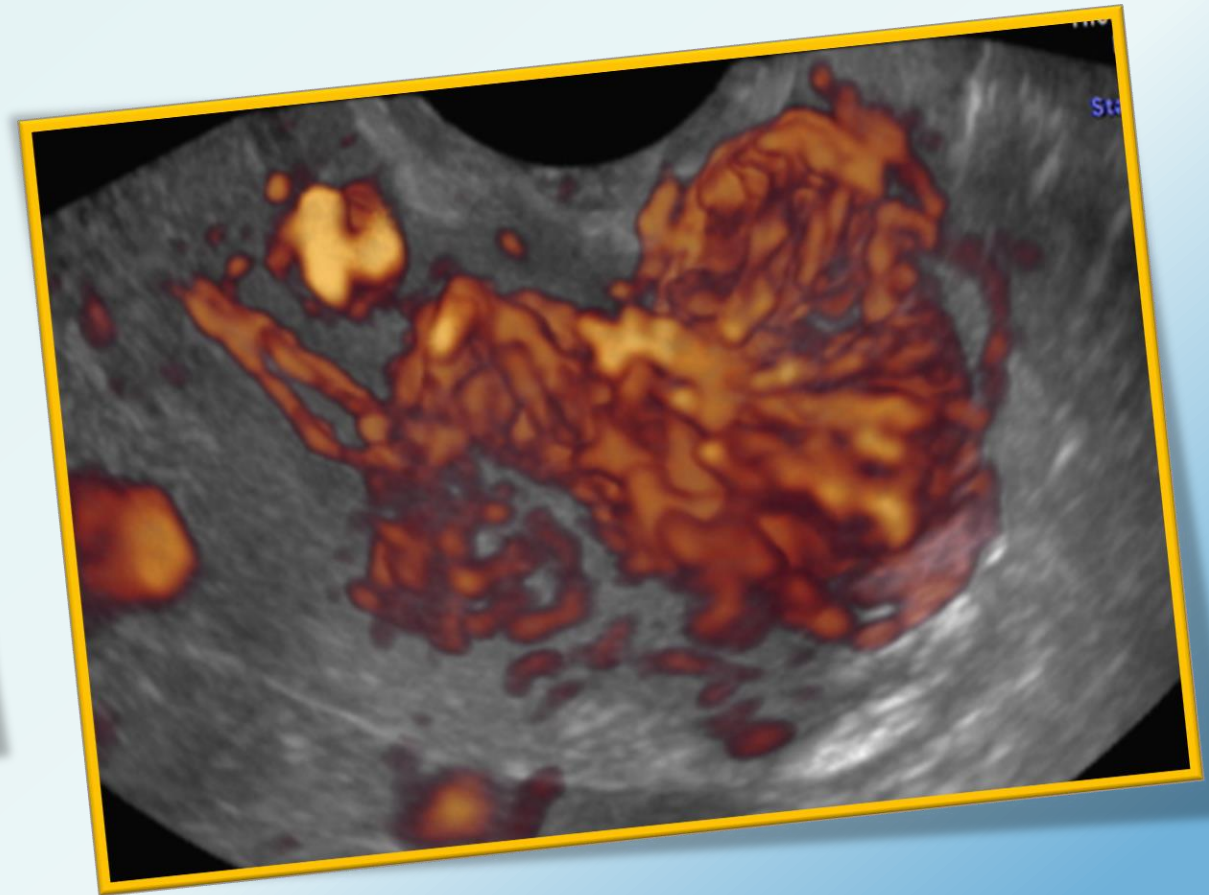
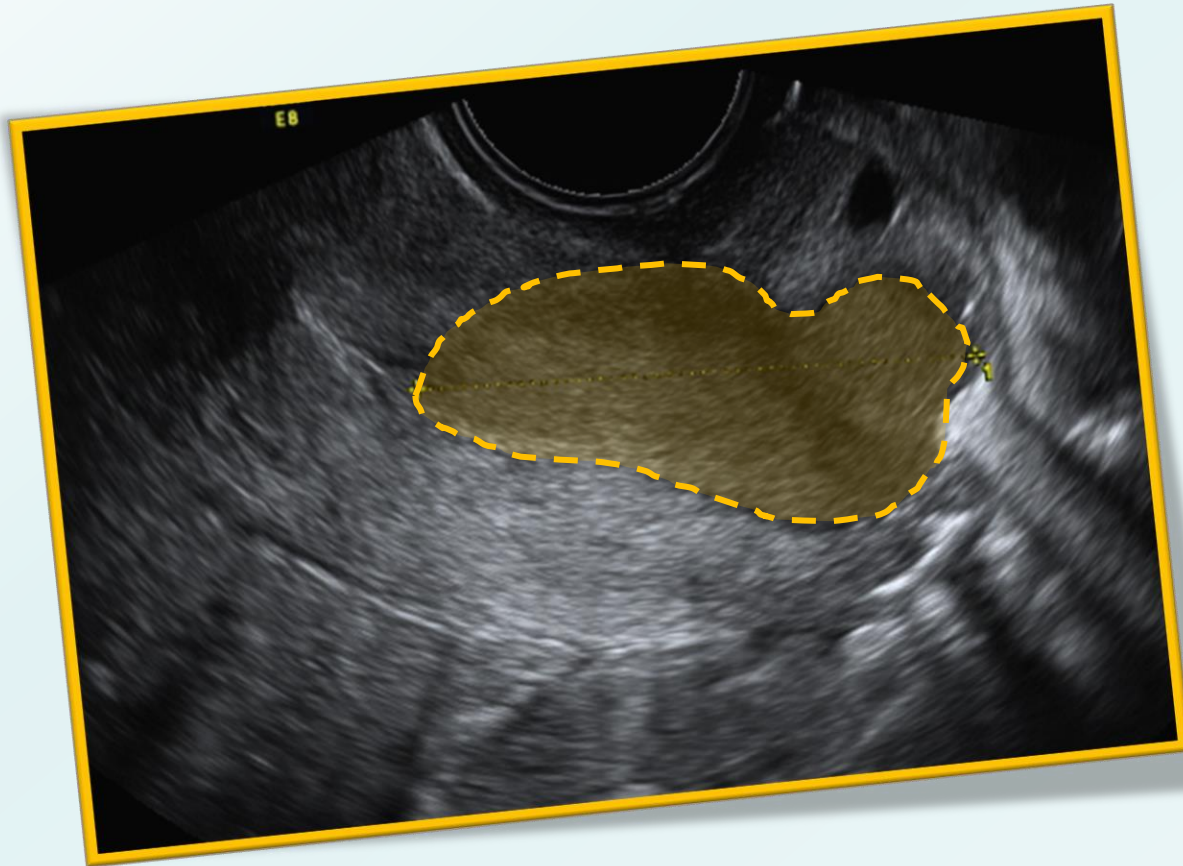
Elisabeth Epstein <sup>a,\*</sup>, Antonia Testa <sup>b</sup>, Adrius Gaurilcikas <sup>c</sup>, Alessia Di Legge <sup>b</sup>, Liveke Ameye <sup>d</sup>, Vaida Atstupenaite <sup>e</sup>, Anna Lia Valentini <sup>f</sup>, Benedetta Gui <sup>f</sup>, Nils-Olof Wallengren <sup>g</sup>, Sonja Pudaric <sup>g</sup>, Arvydas Cizauskas <sup>h</sup>, Anna Måsbäck <sup>i</sup>, Gian Franco Zannoni <sup>j</sup>, Päivi Kannisto <sup>k</sup>, Michal Zikan <sup>l</sup>, Ivana Pinkavova <sup>l</sup>, Andrea Burgetova <sup>m</sup>, Pavel Dundr <sup>n</sup>, Kristyna Nemejcova <sup>n</sup>, David Cibula <sup>l</sup>, Daniela Fischerova <sup>l</sup>

182 early-stage cervical cancers.

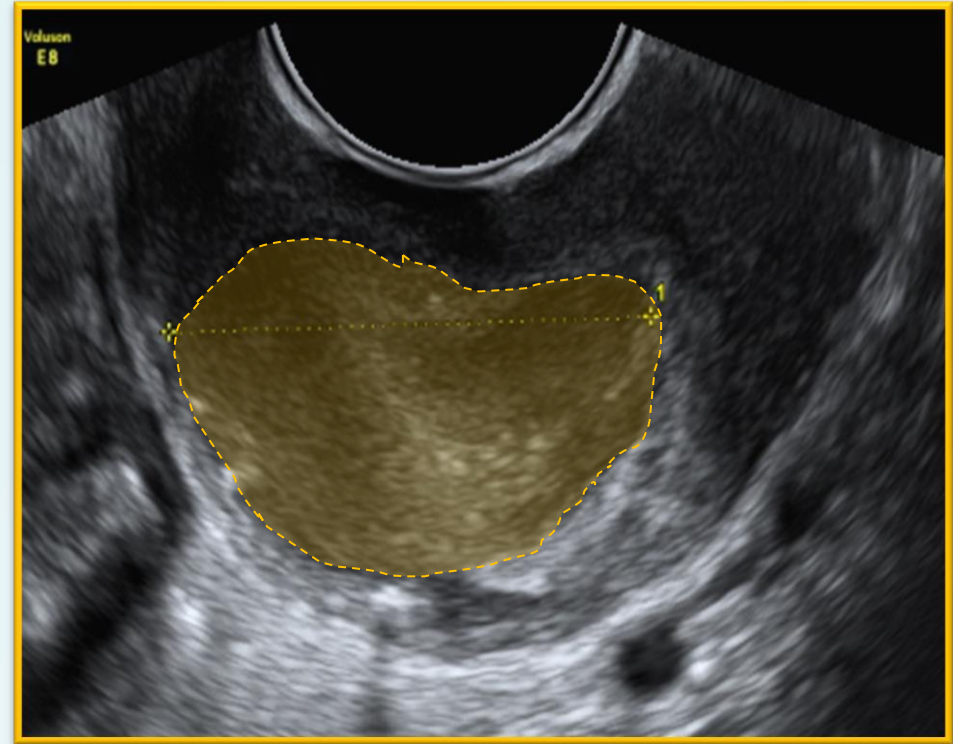
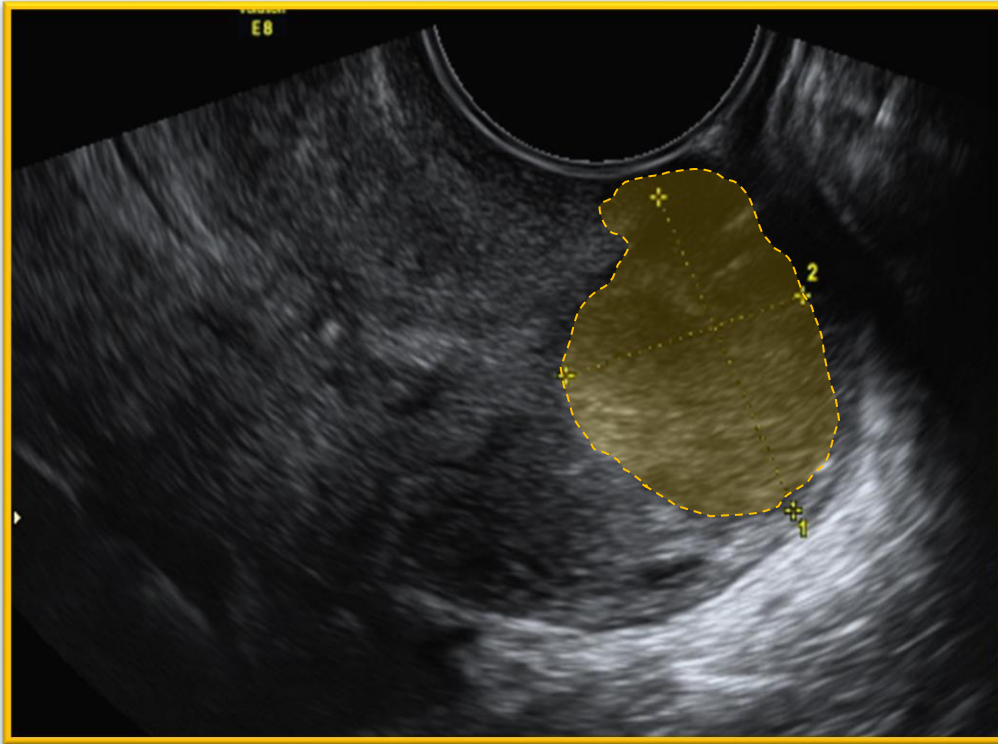
TVS > MRI in tumor detection.

TVS = MRI for parametrial involvement and stromal invasion >2/3.

# How can we assess cervical cancer by TVUS - TRUS?



# What should be assessed by TVUS - TRUS?

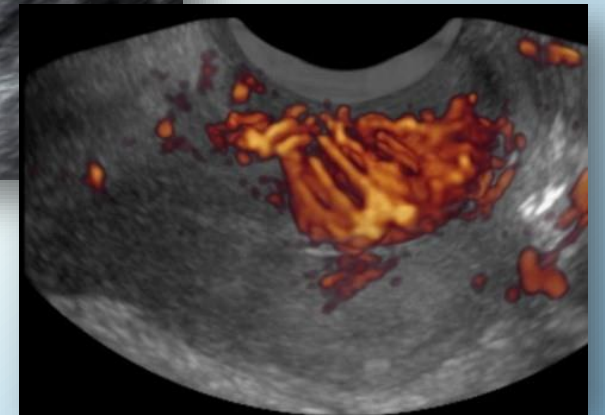
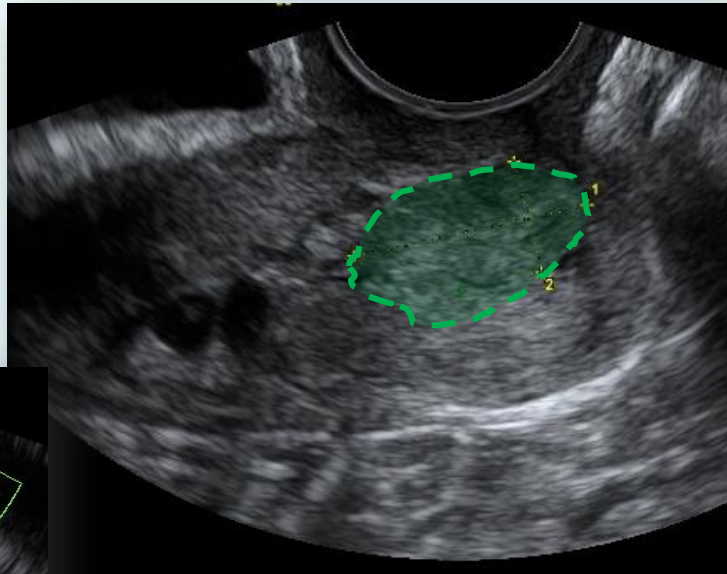


Presence of disease



# Sonographic characteristics of squamous cell cancer (SCC) and adenocarcinoma of the uterine cervix (AC) at TVUS

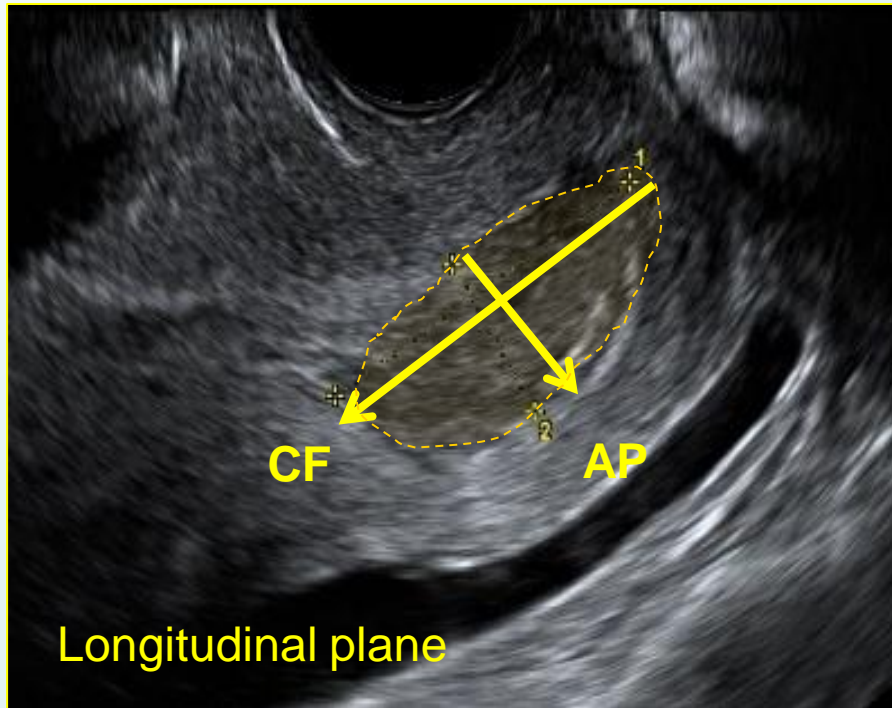
Prospective two center study 40 pts (20 SCC, 20 AC)



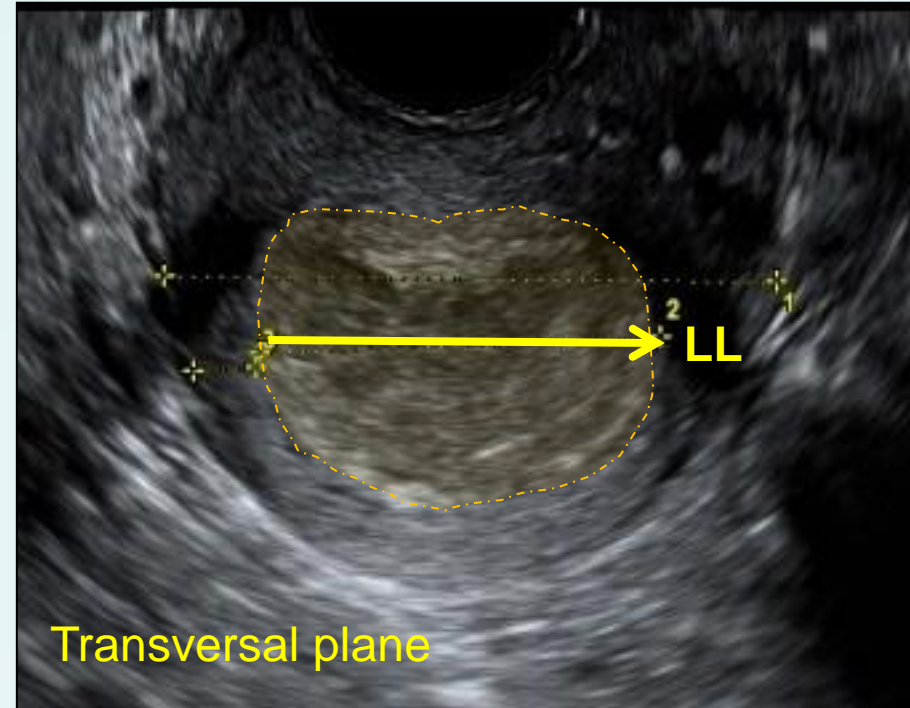
Isoechoic echogenicity associated with AC in 68%

Hypoechoic echogenicity associated with SCC in 73%

# Tumor measurement



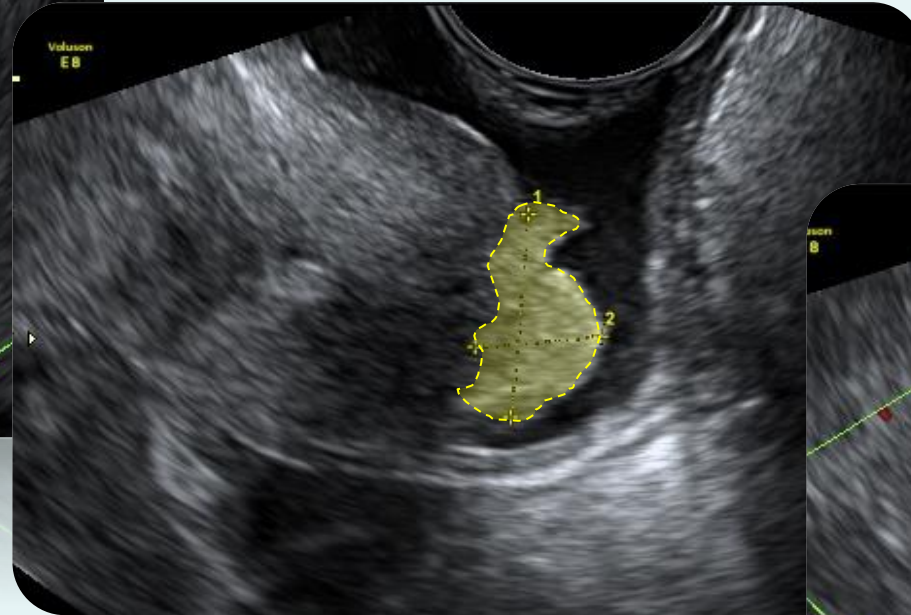
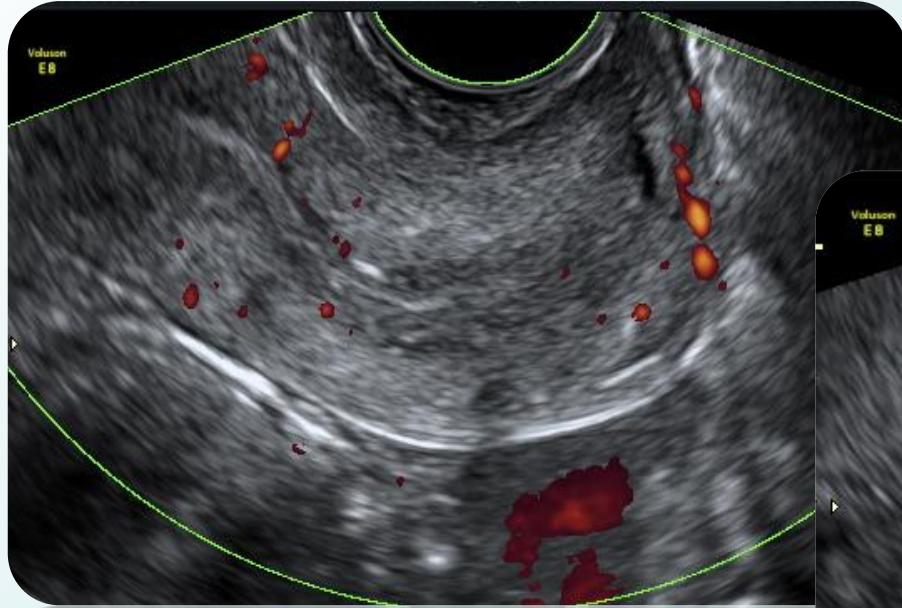
Longitudinal plane:  
Cervical fundal (CF)  
Antero-posterior (AP)



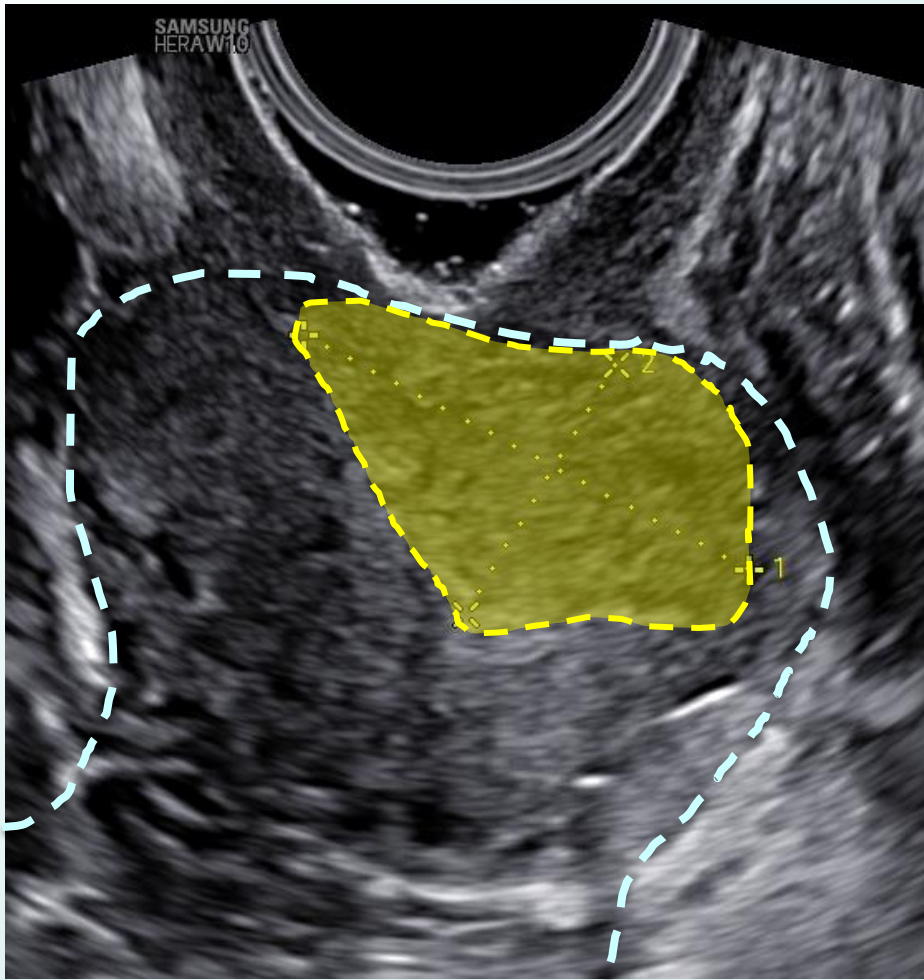
Transversal Plane:  
Lateral-lateral (LL)

Maximal tumor diameter  $<$  or  $>$  4 cm

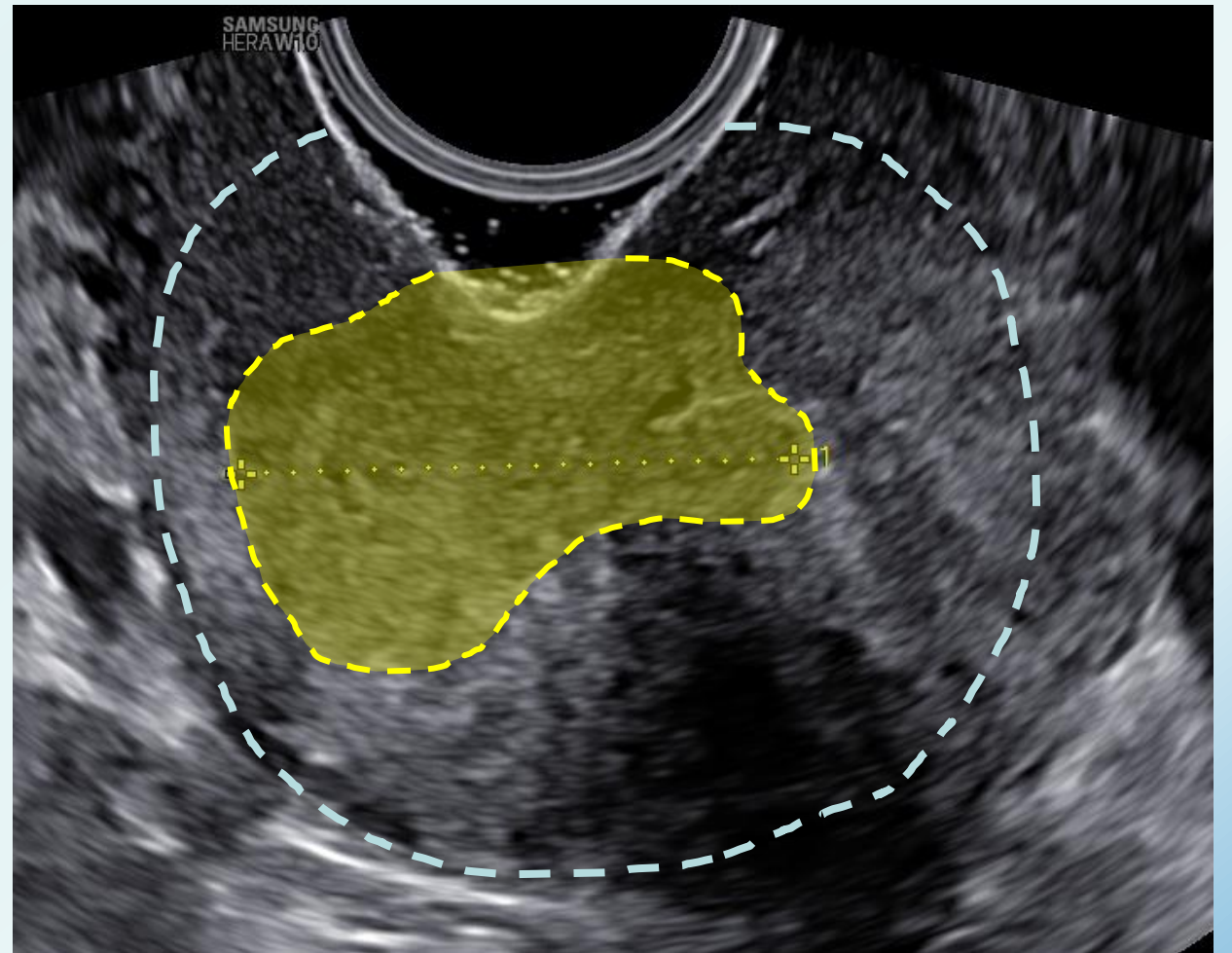
# The role of vaginosonography



Suitable for small and /or  
mainly exophytic lesions

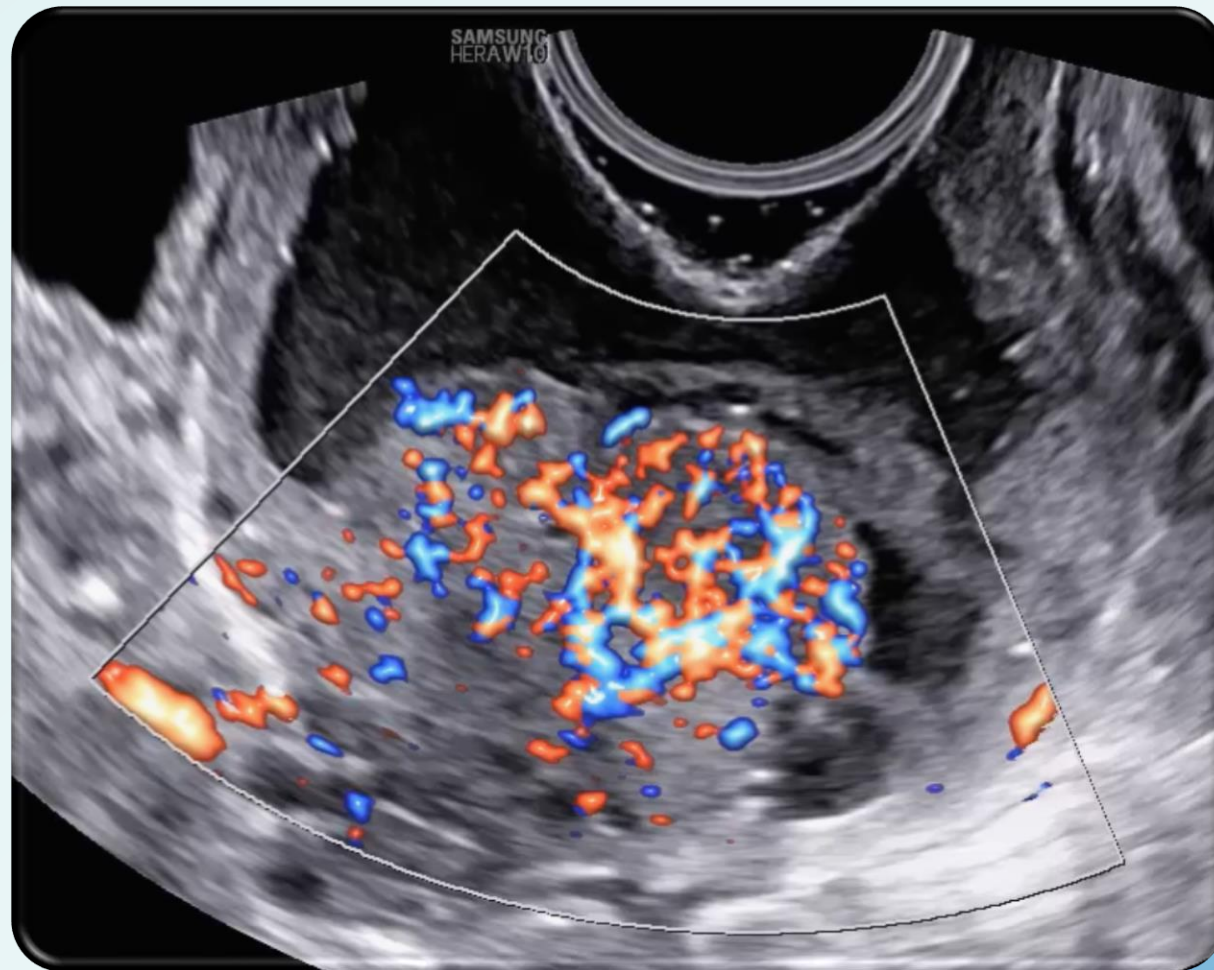


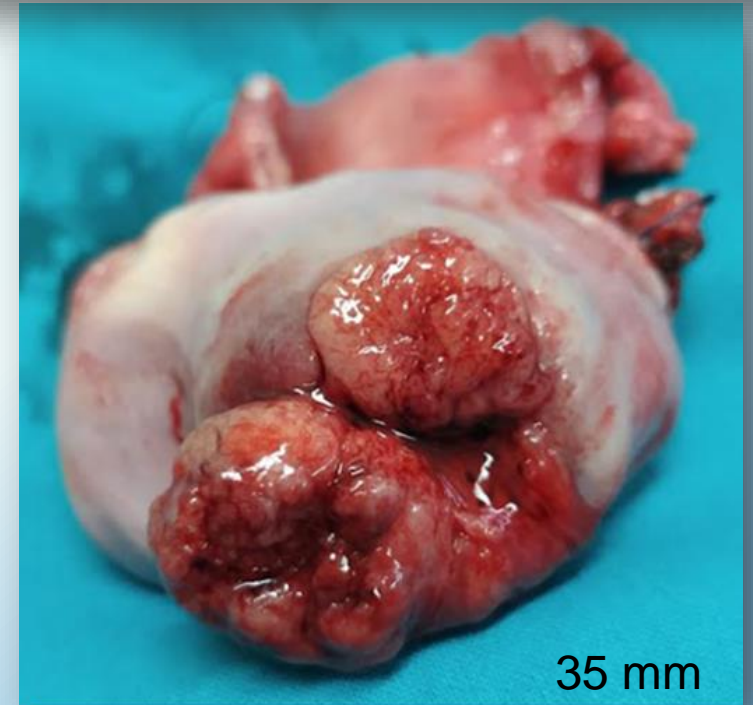
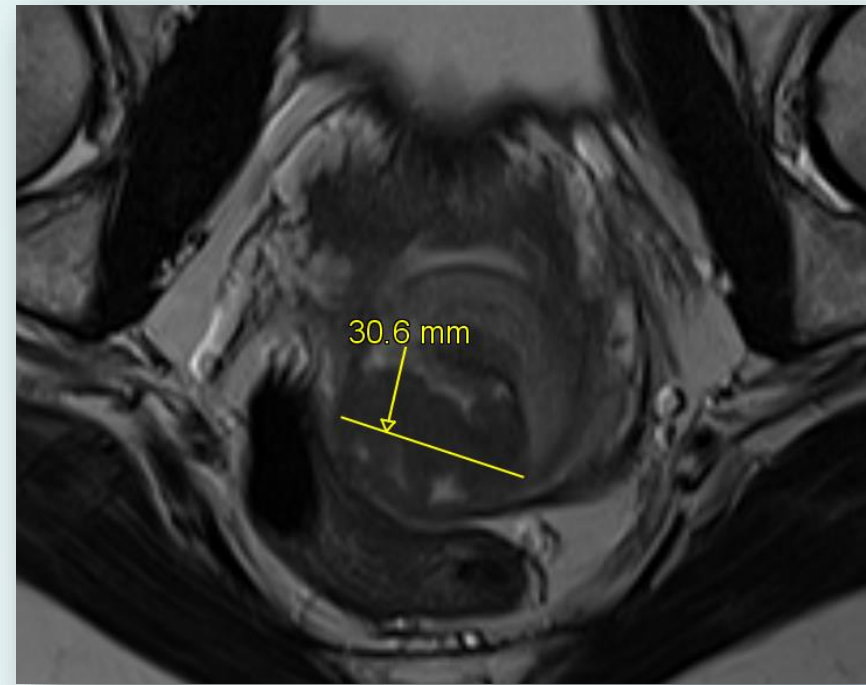
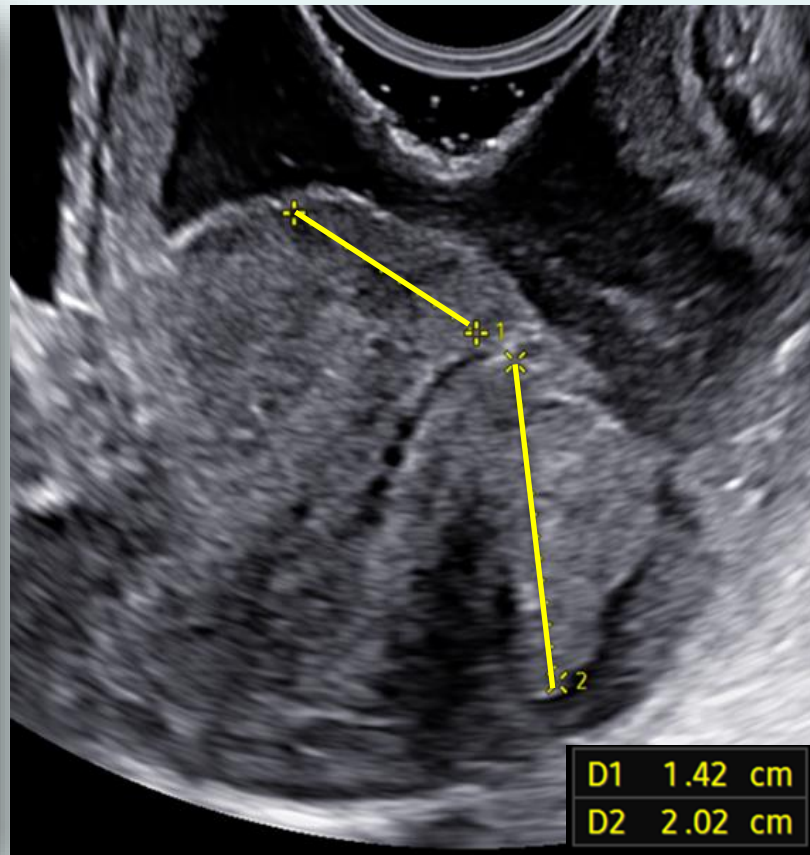
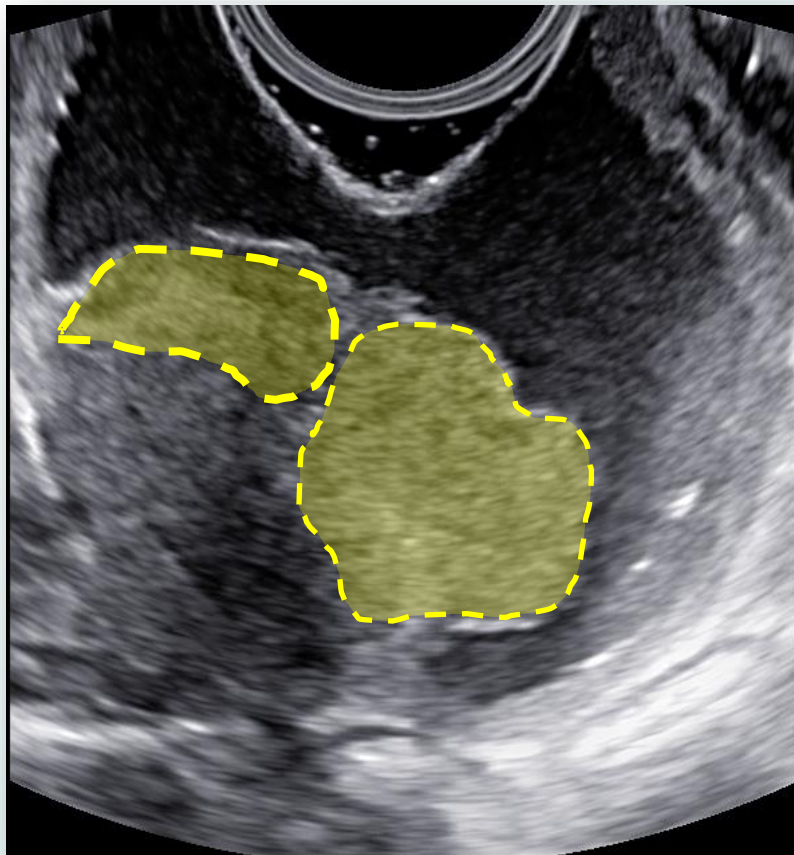
Long section



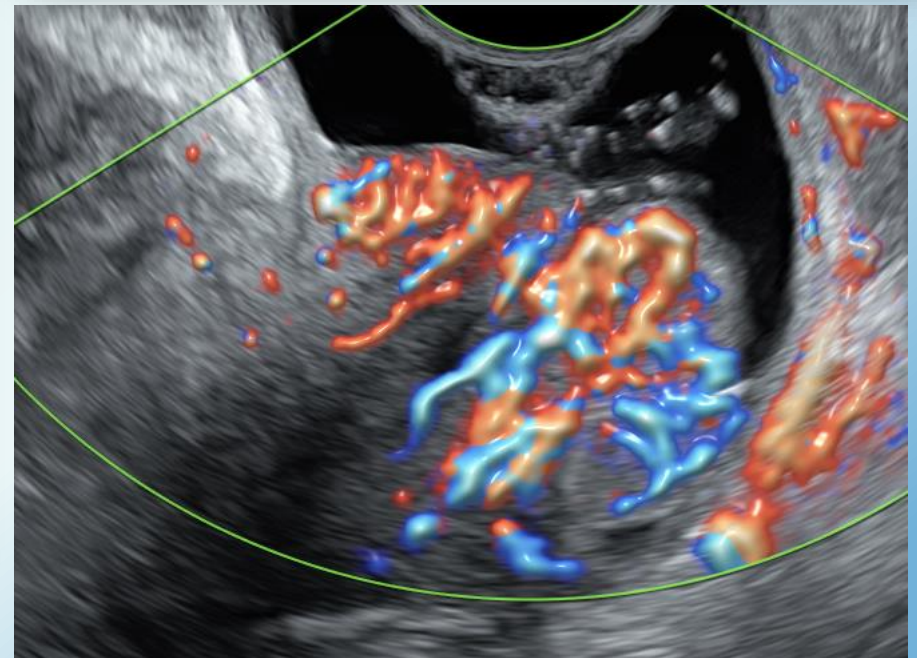
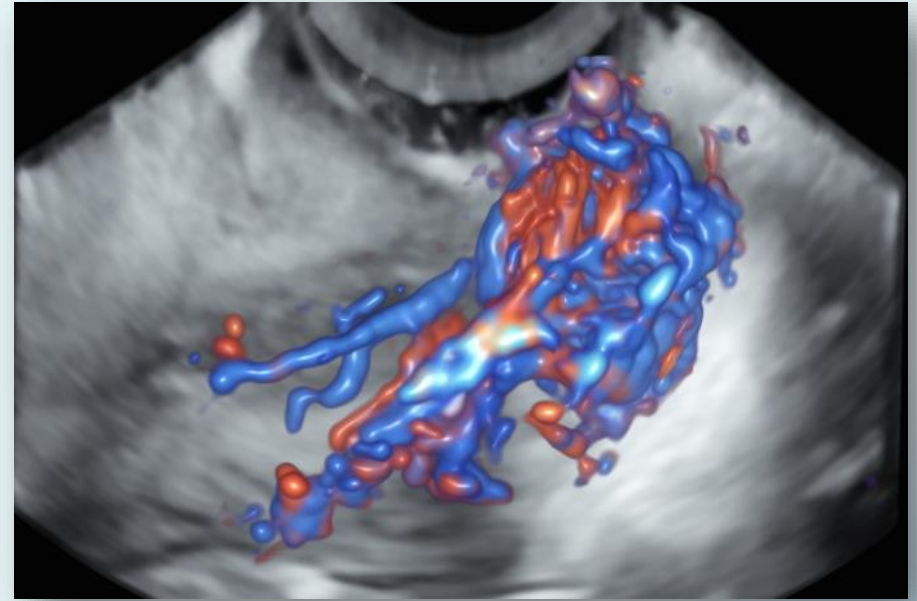
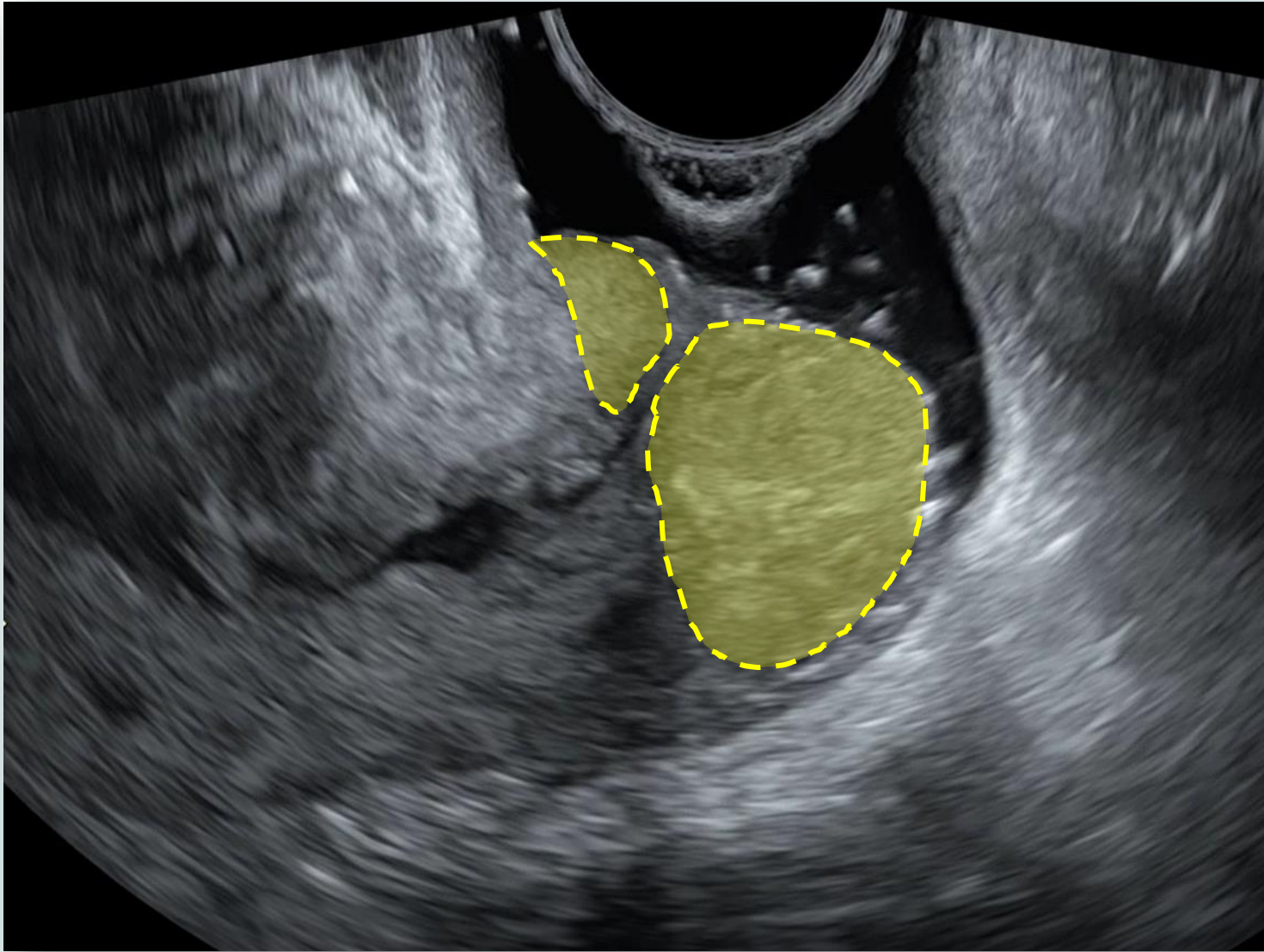
Transverse section

Age 38 yrs

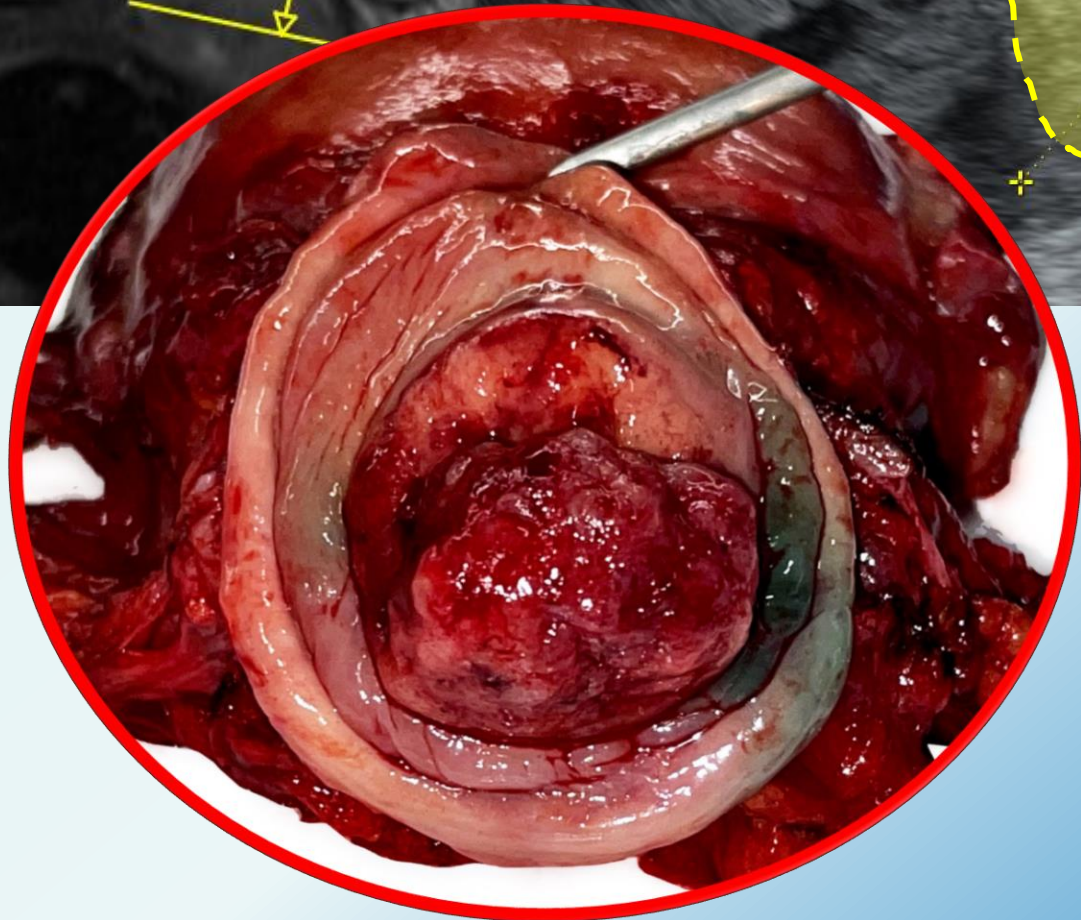
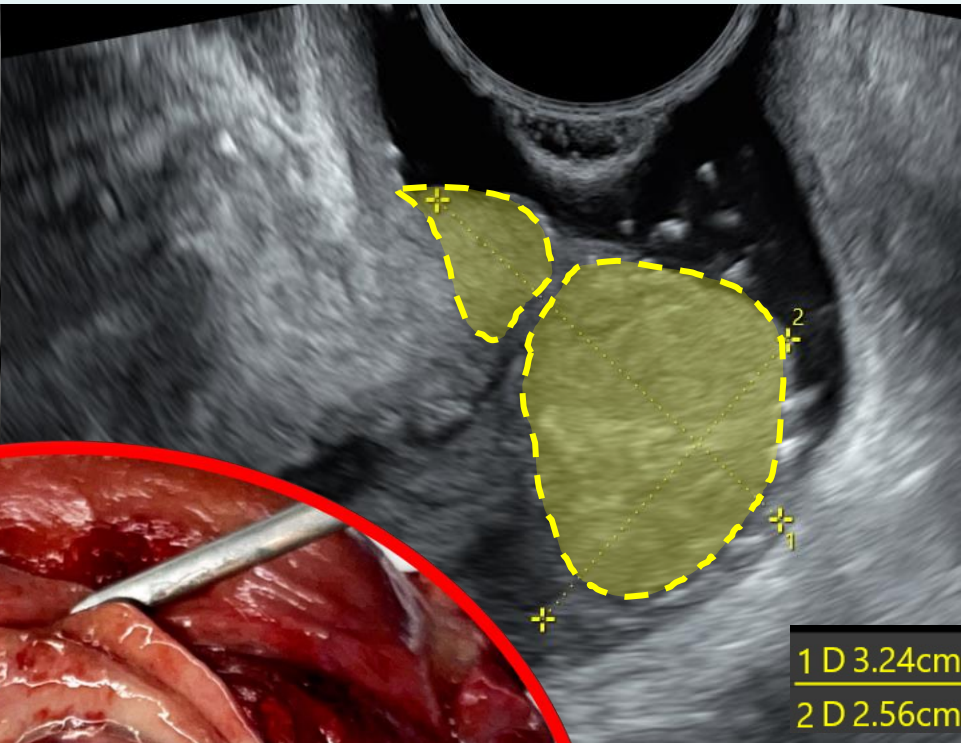
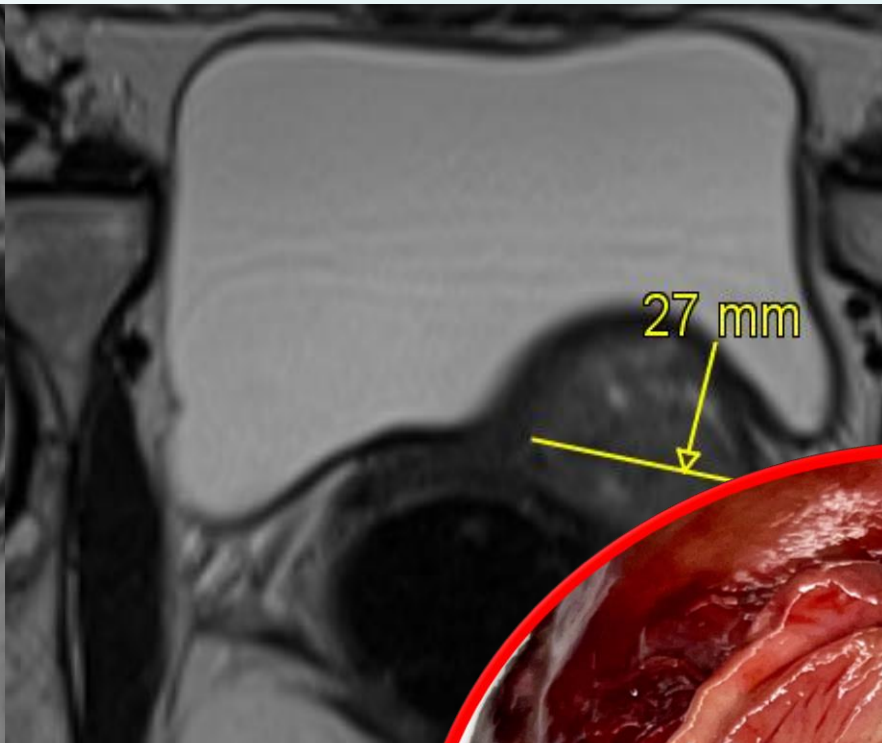
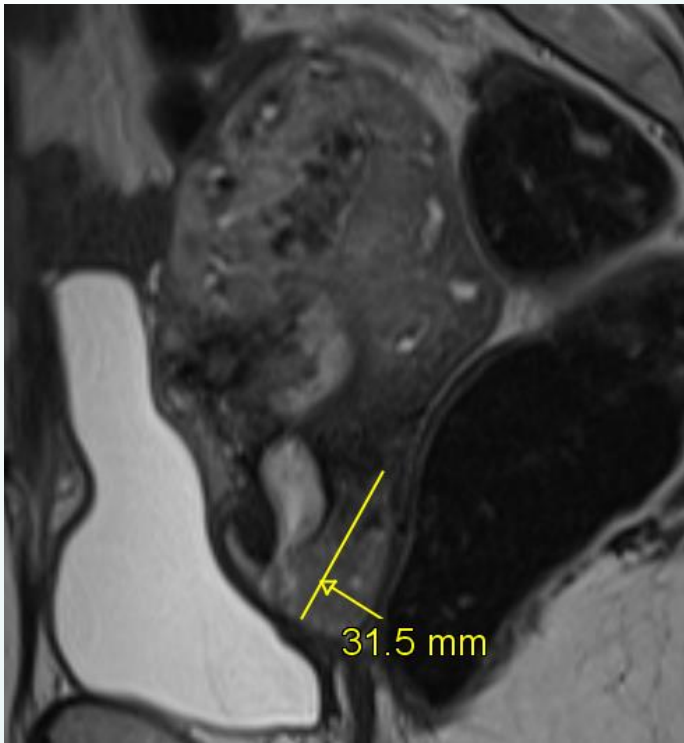




Squamous cervical cancer  
stage pT1b2  
IIIC1 Pelvic N+



Age 34



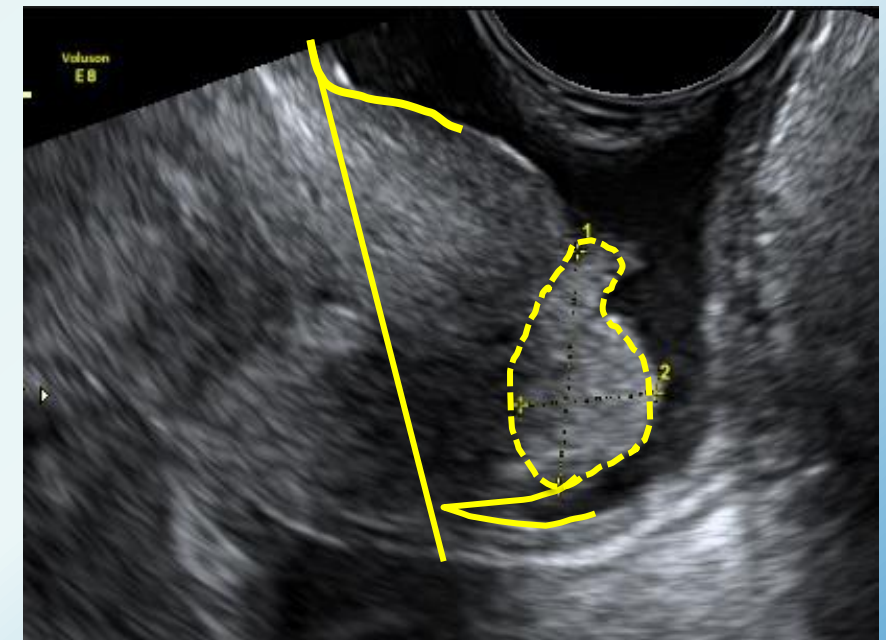
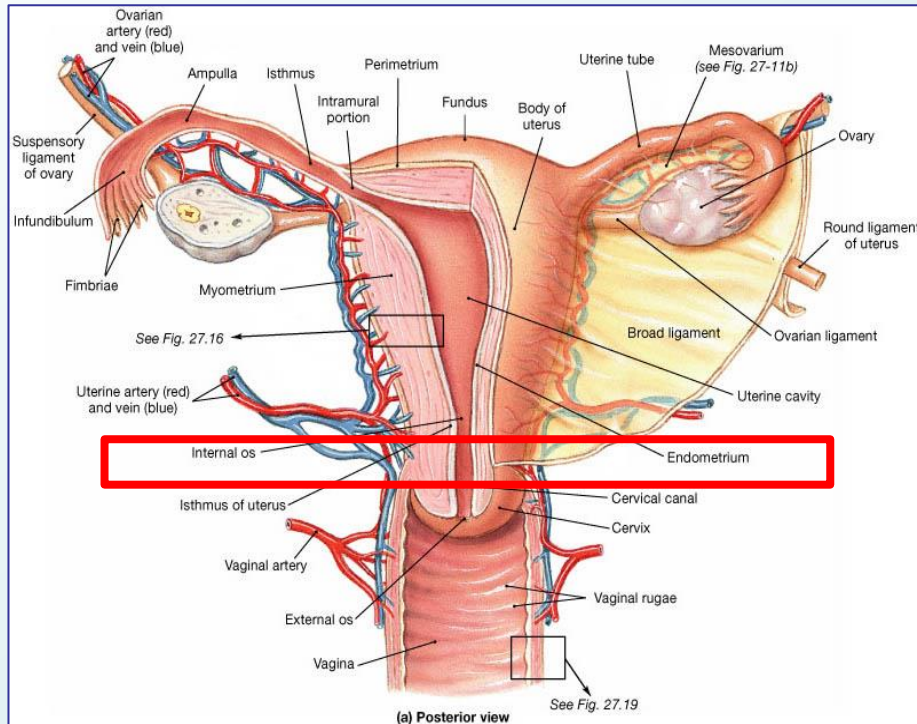
**Cesarean Section 32+5 w for suspicious placental abruption**

**SCC IB2 diam at MRI 31x27x18**



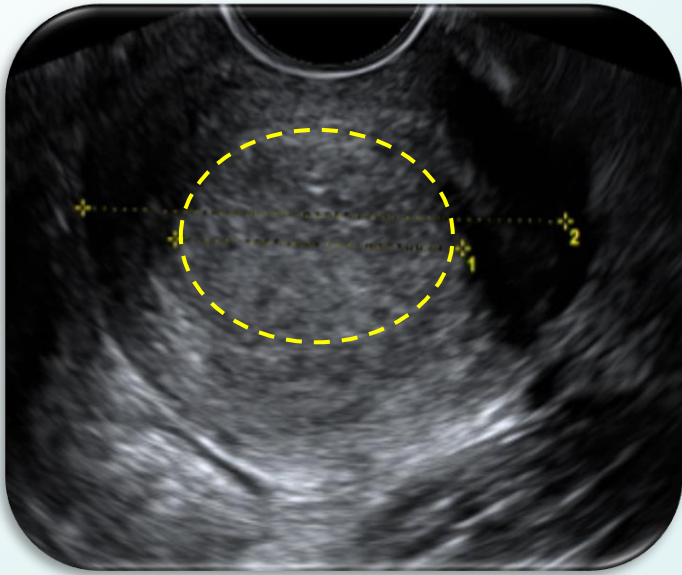
# Assessment of stromal invasion & parametrial invasion

Stromal and lateral parametrial invasion should be assessed at the level where uterine arteries arrive = above vaginal fornices

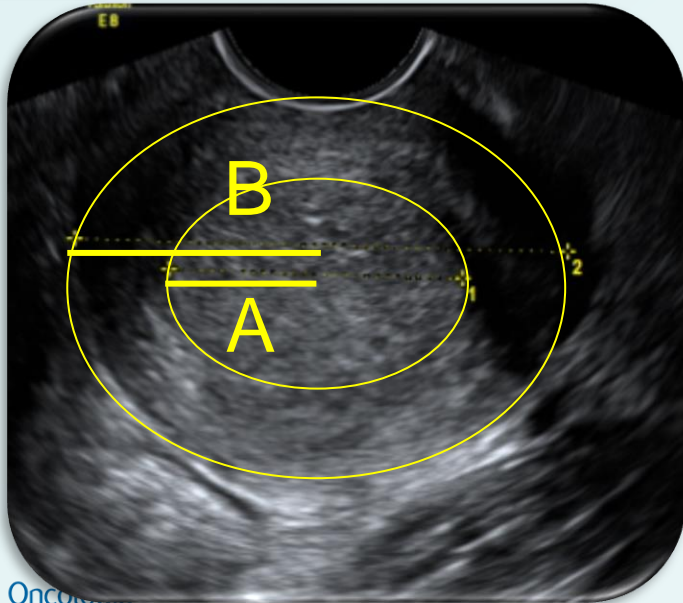


- Exophytic tumors growth below fornices
- no risk of parametrial invasion
- don't forget to look for vaginal/paracolpic extension

# Assessment of stromal invasion (transverse section)

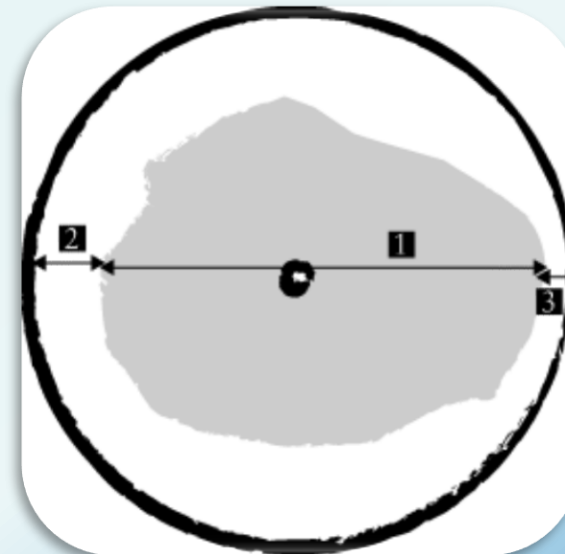
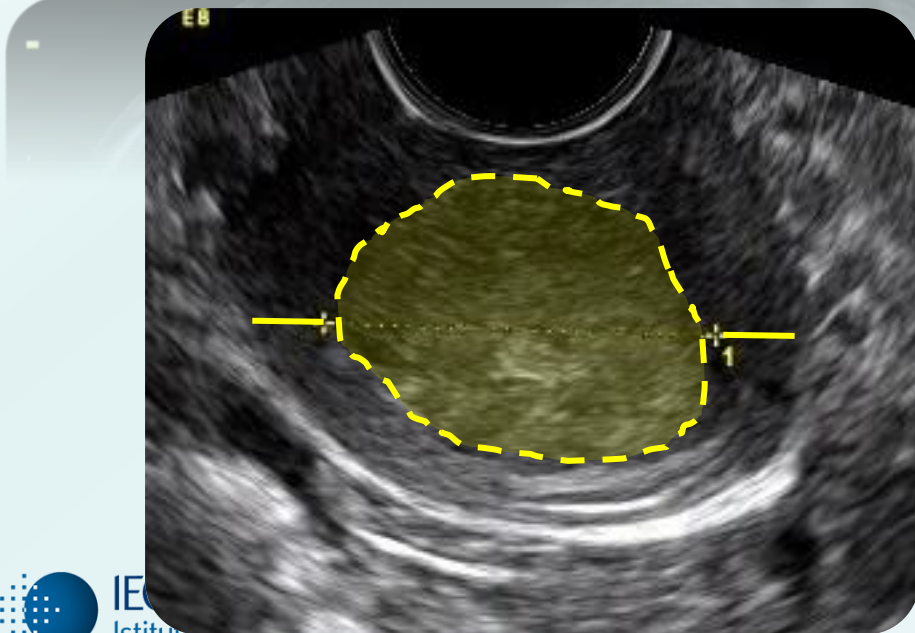
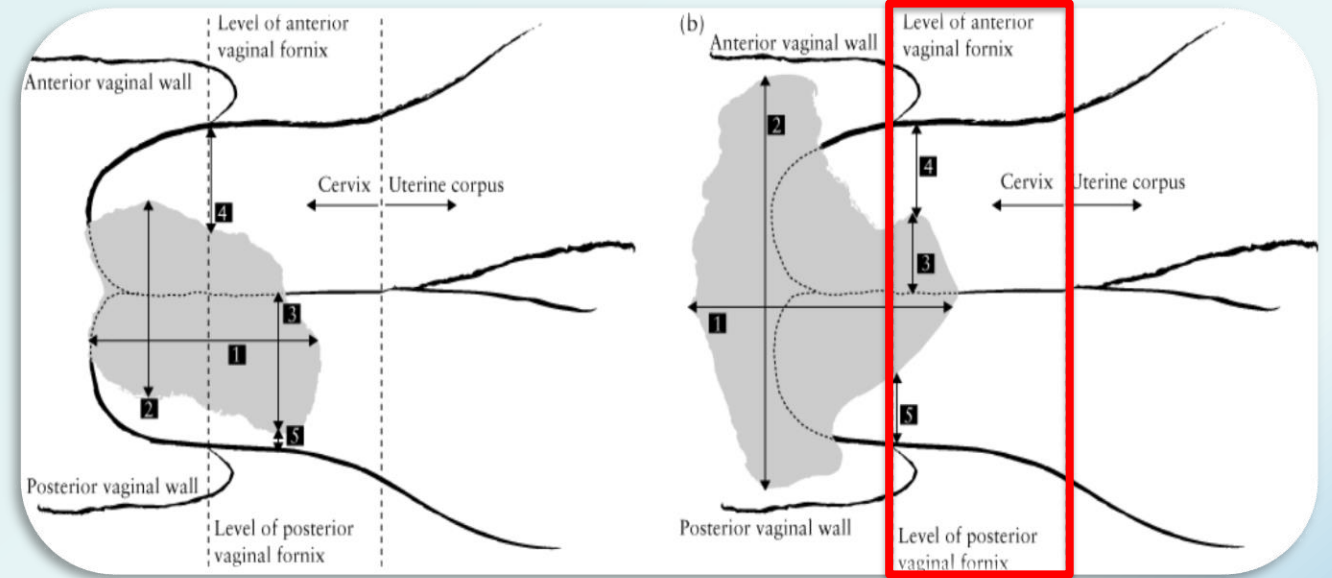
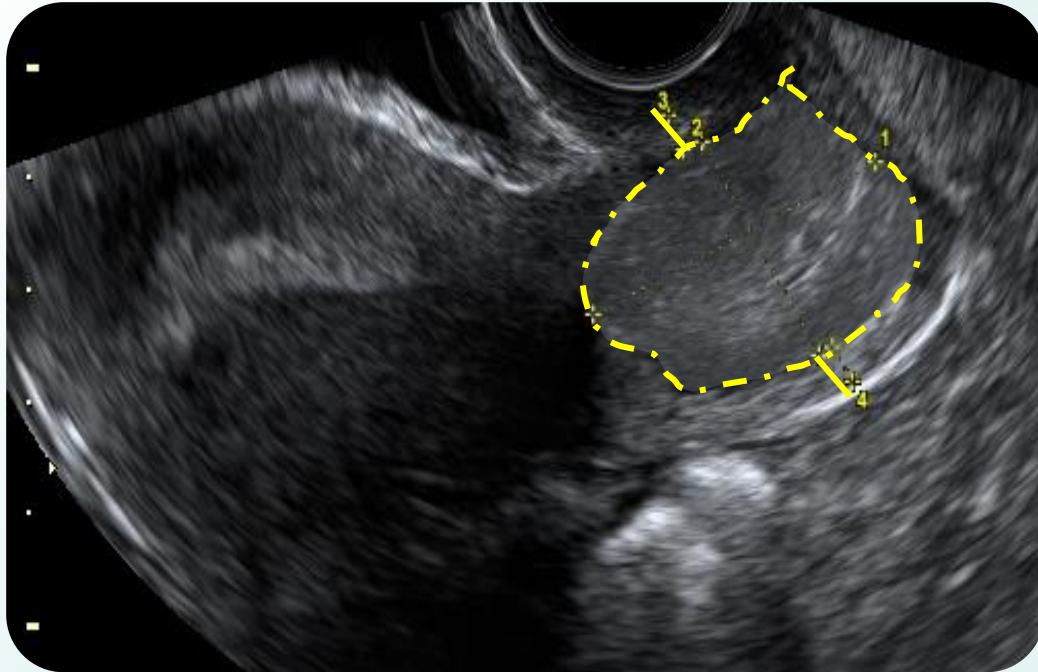


Assess if stromal invasion  $< 2/3$  or  $\geq 2/3$  on right and left side

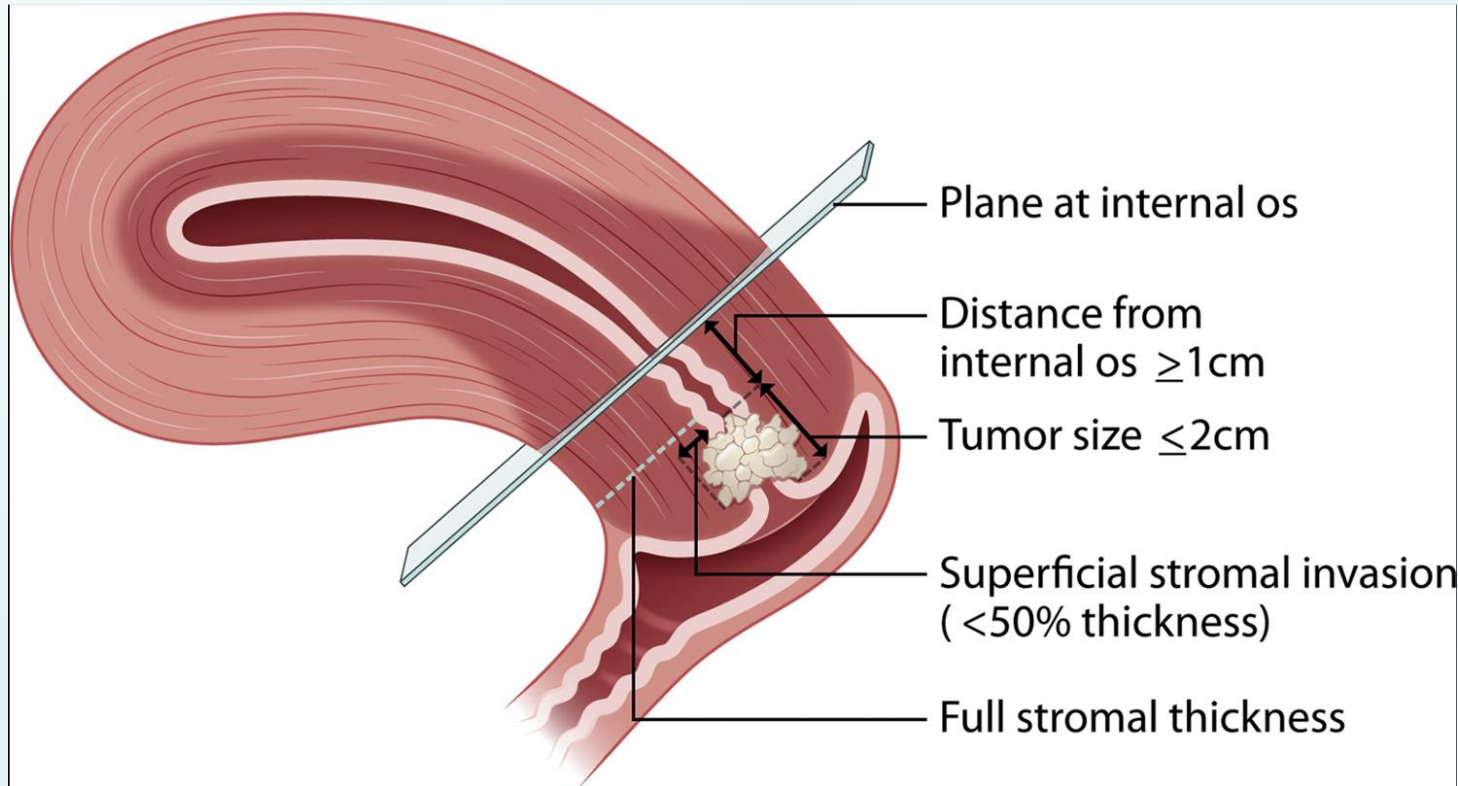


One wall max tumor diameter (A) /  
One wall cervical diameter (B)

# Minimum Free Margin > 3 mm

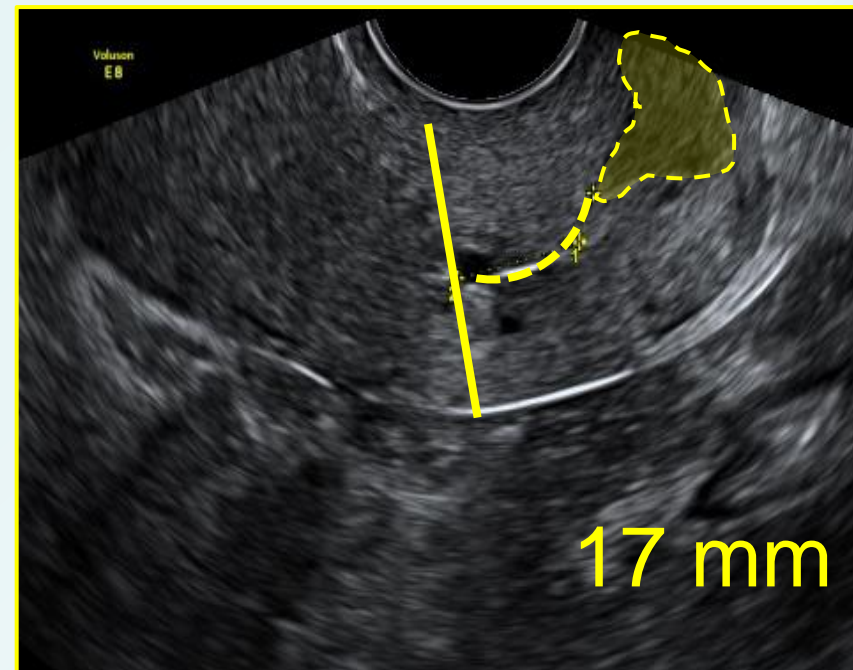
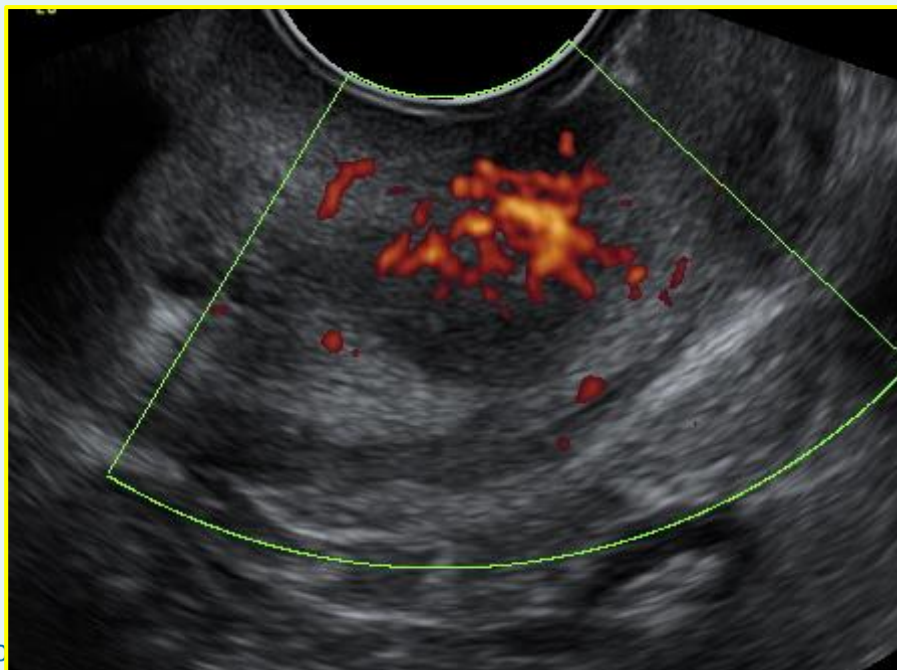
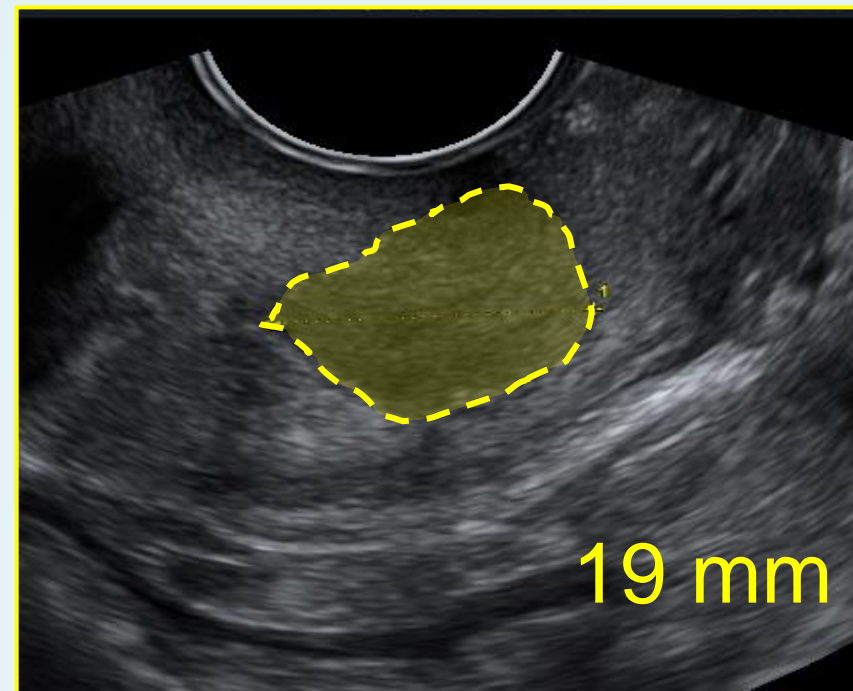
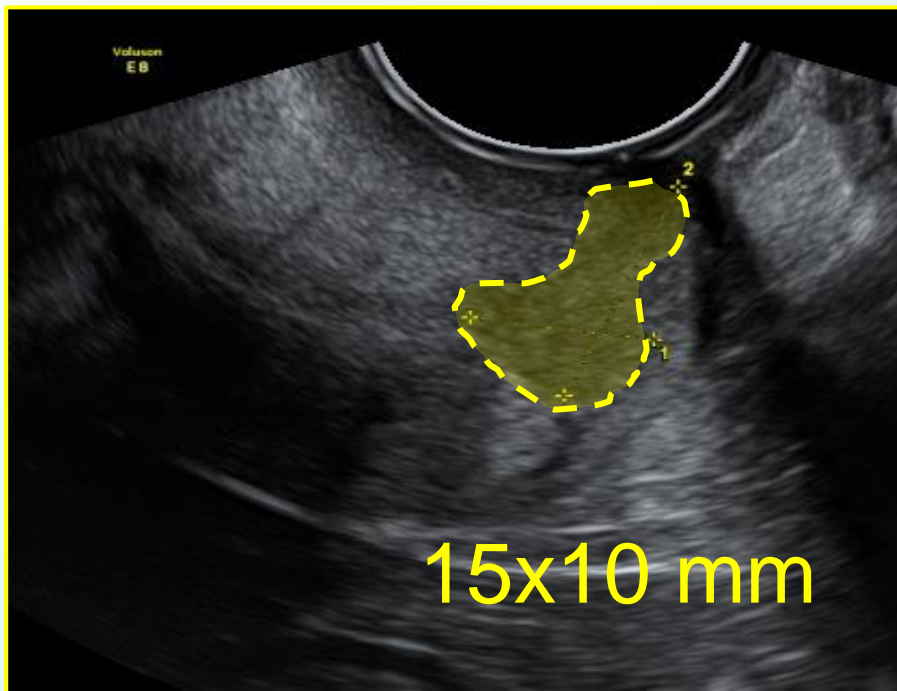


# Assessment of minimal distance upper margin of tumor to inner cervical os

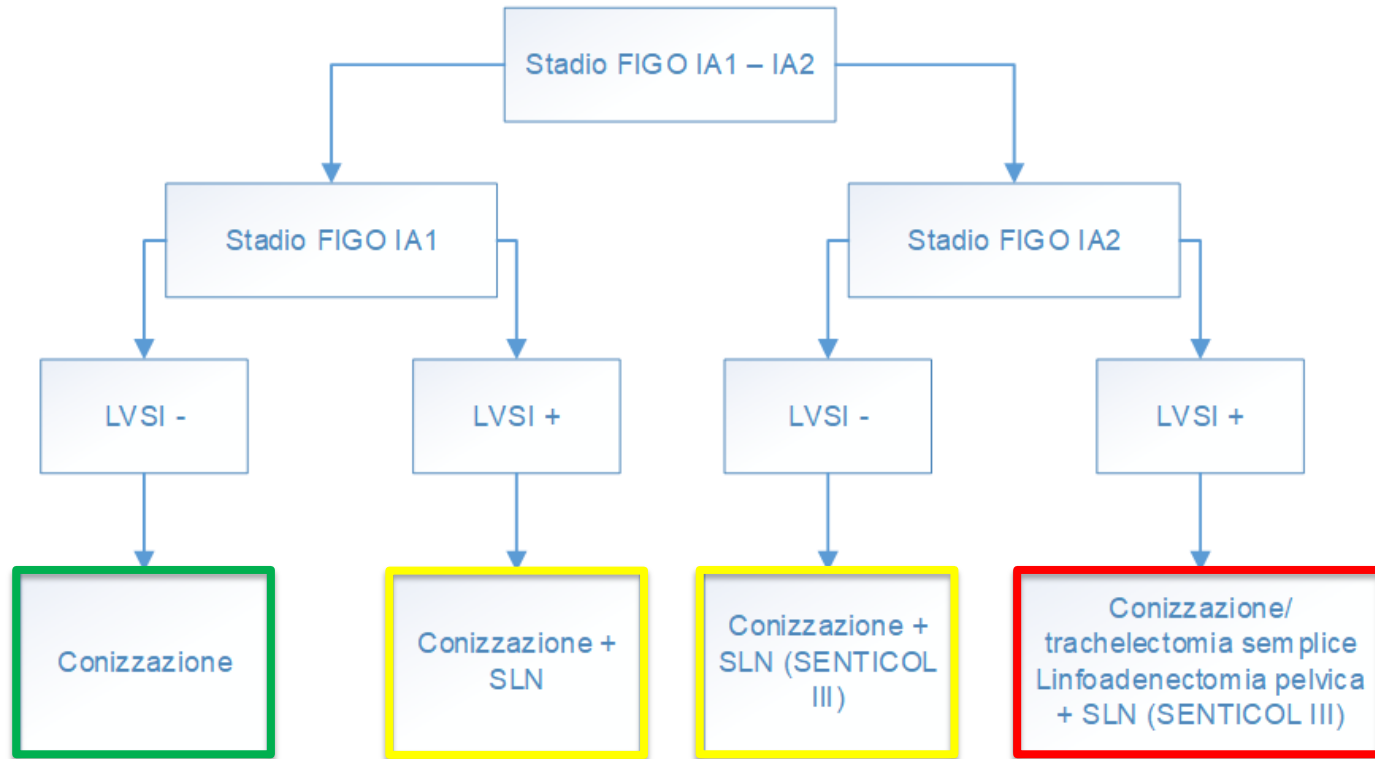


Trachelectomy or conization:  
Tumors  $< 2\text{ cm}$ ,  
Distance tumor to inner  
cervical os  $\geq 1\text{ cm}$

Distance highest margin of  
tumor to inner cervical os  
(at arrival of uterine arteries )

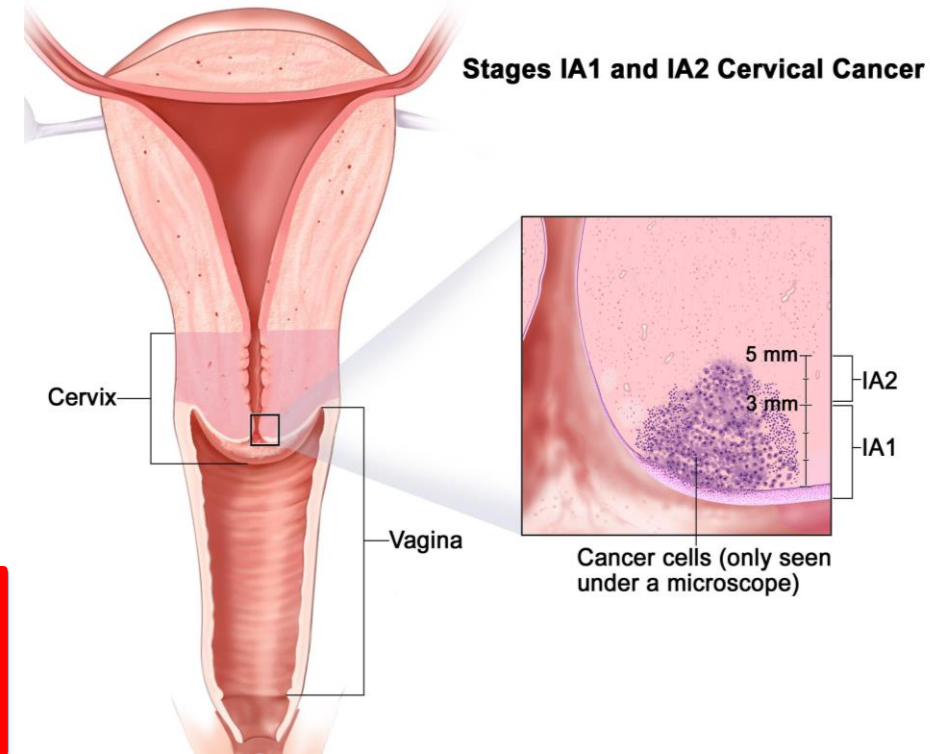


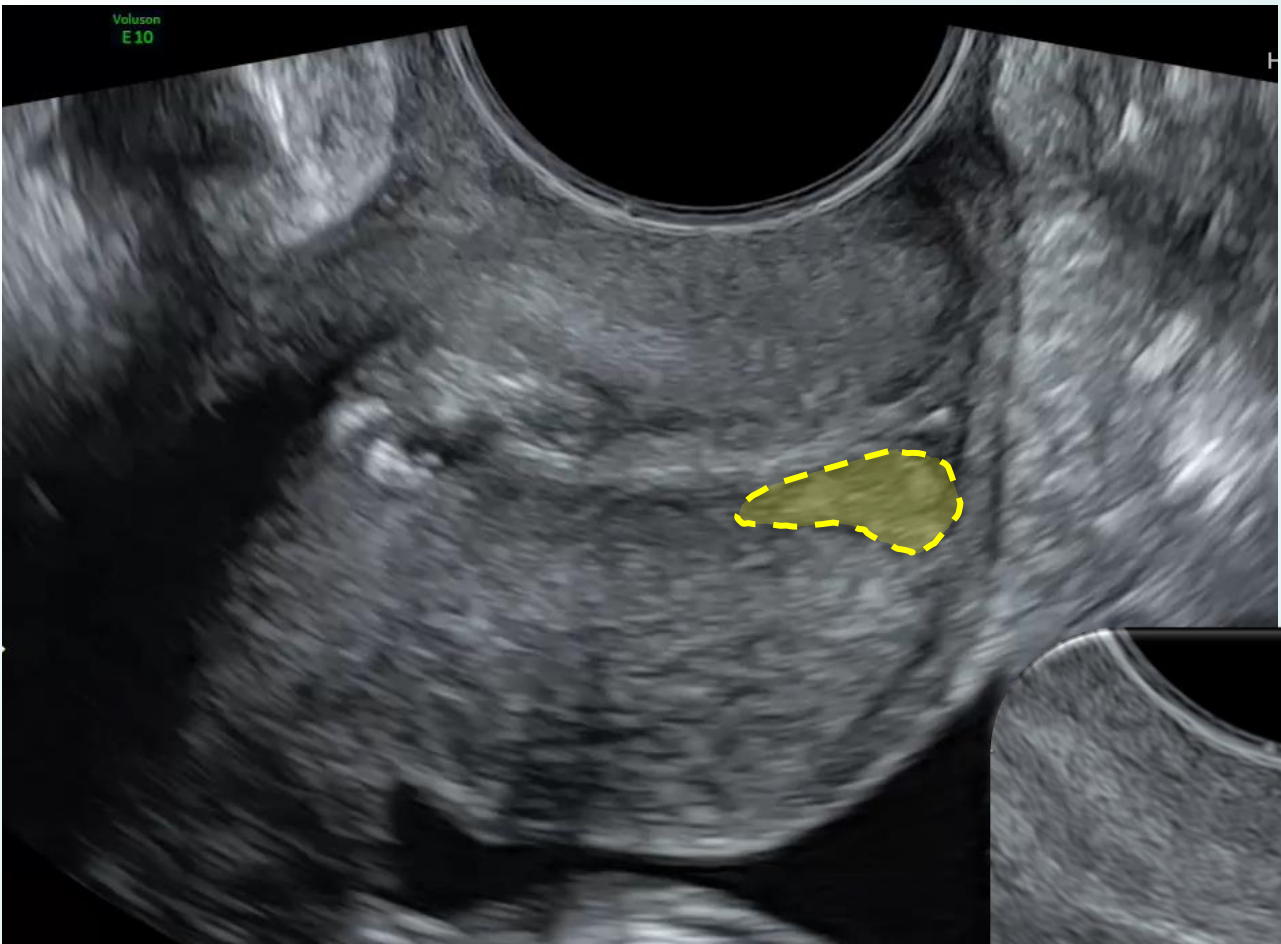
- Desiderio di prole
- Età ≤ 42
- Istotipo: Squamoso – Adenosquamoso Adenocarcinoma



**Linfonodi Positivi: STOP percorso conservativo**

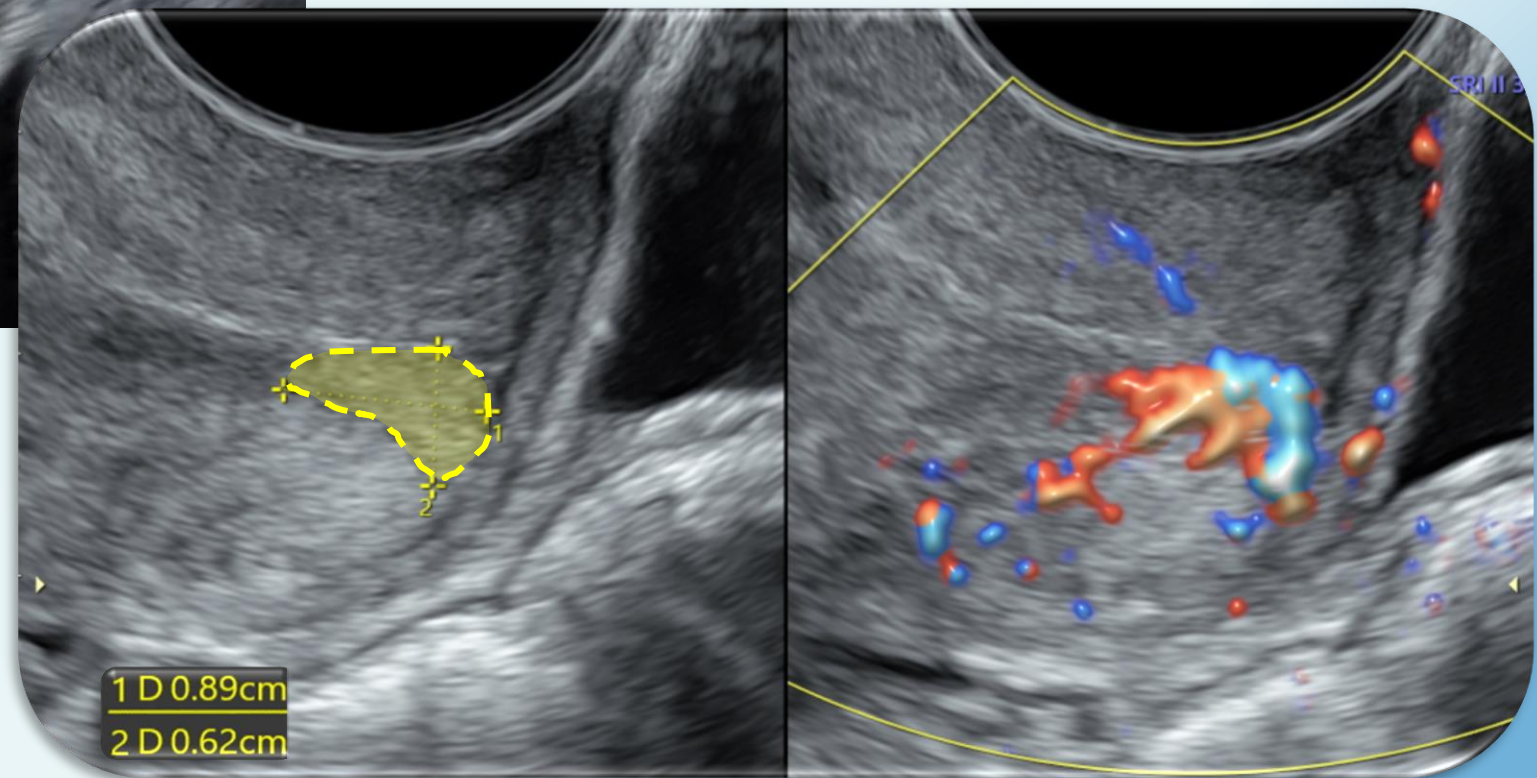
Treatment adjuvant based on risk factors (positive margins on cone, LVSI +)



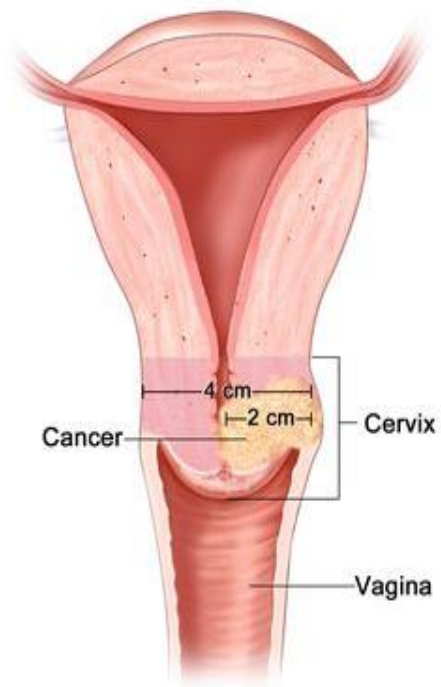


Maximal lenght 9 mm  
Stromal infiltration 1 mm  
Stage IA1 LVSI-

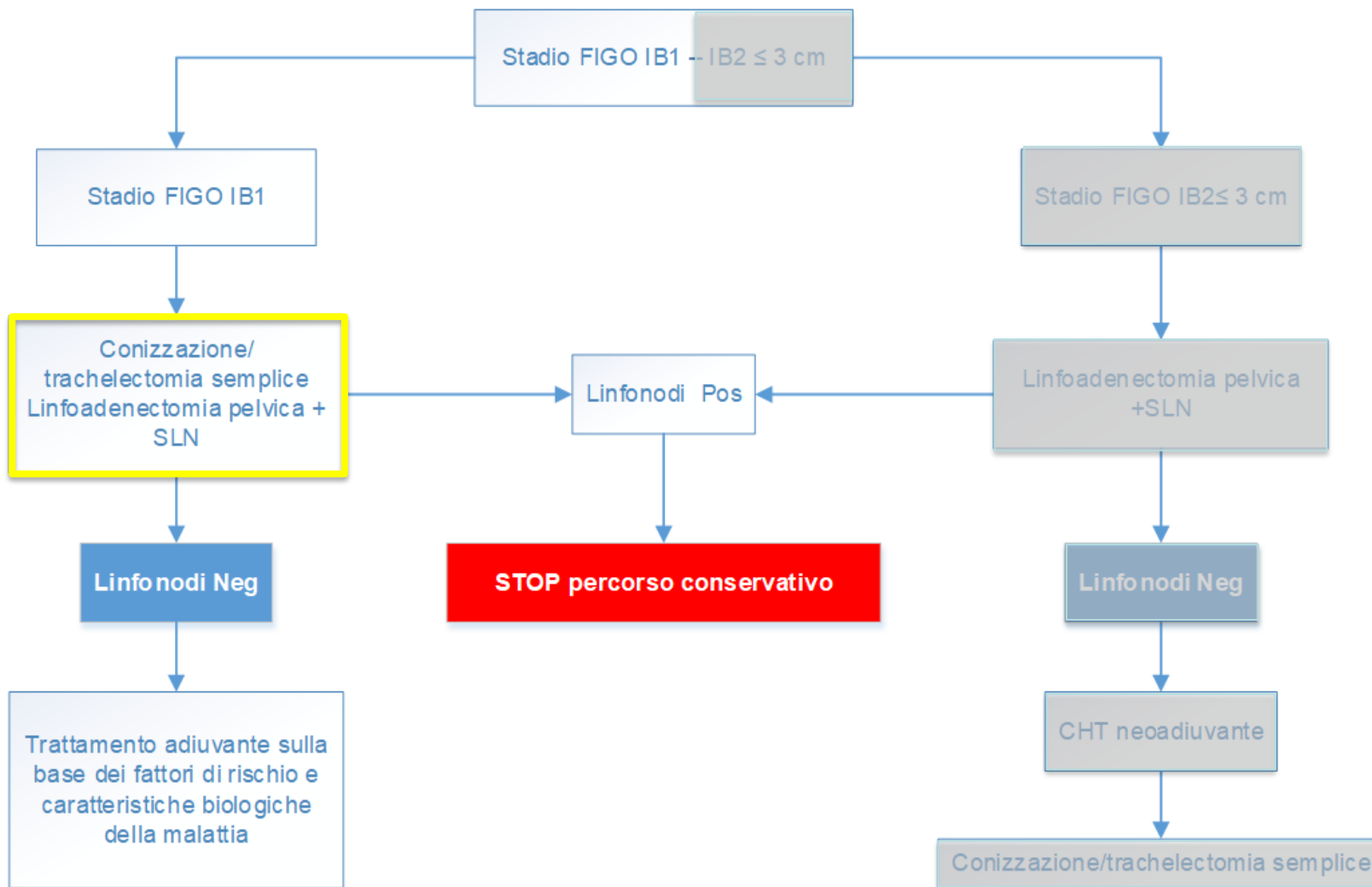
# Laserconization



## FIGO stage IB1



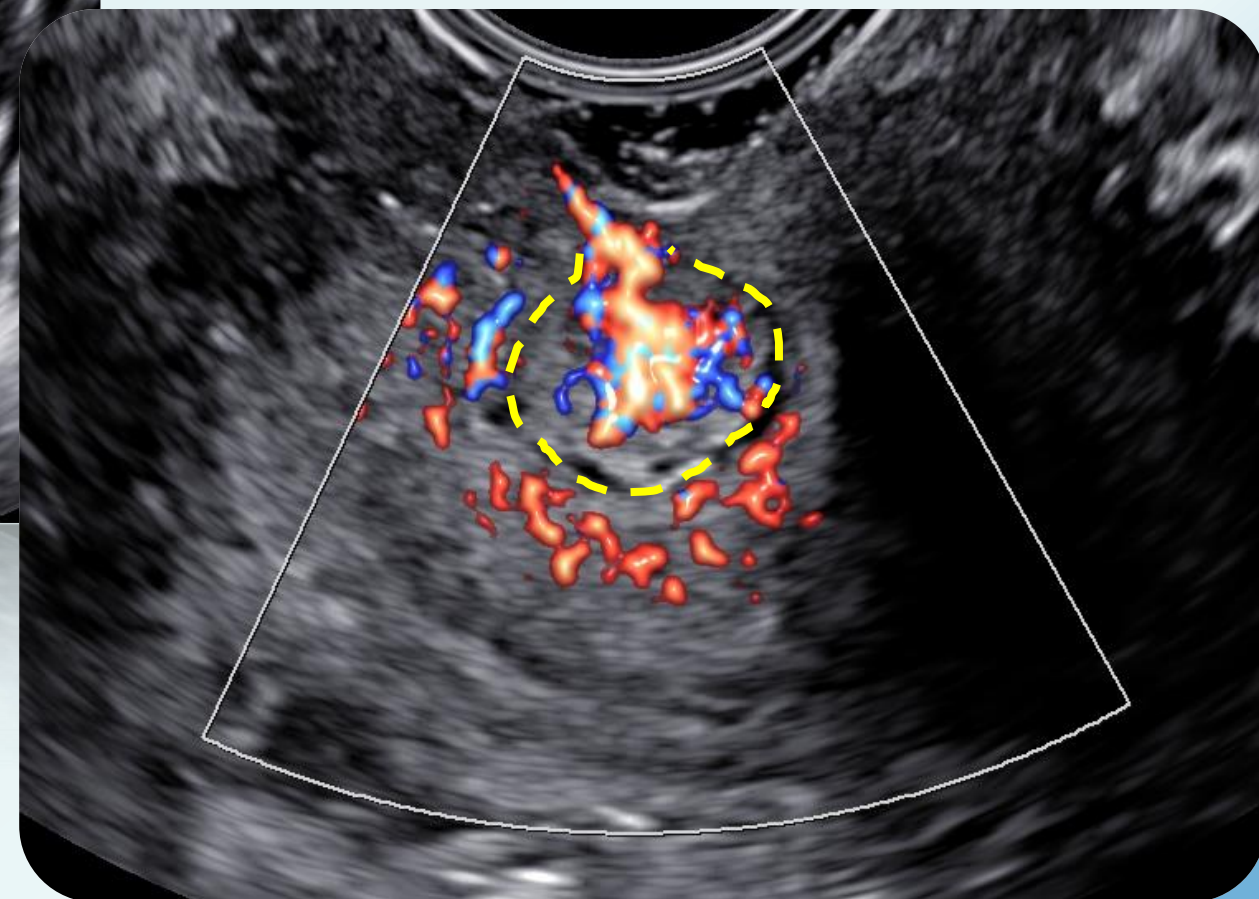
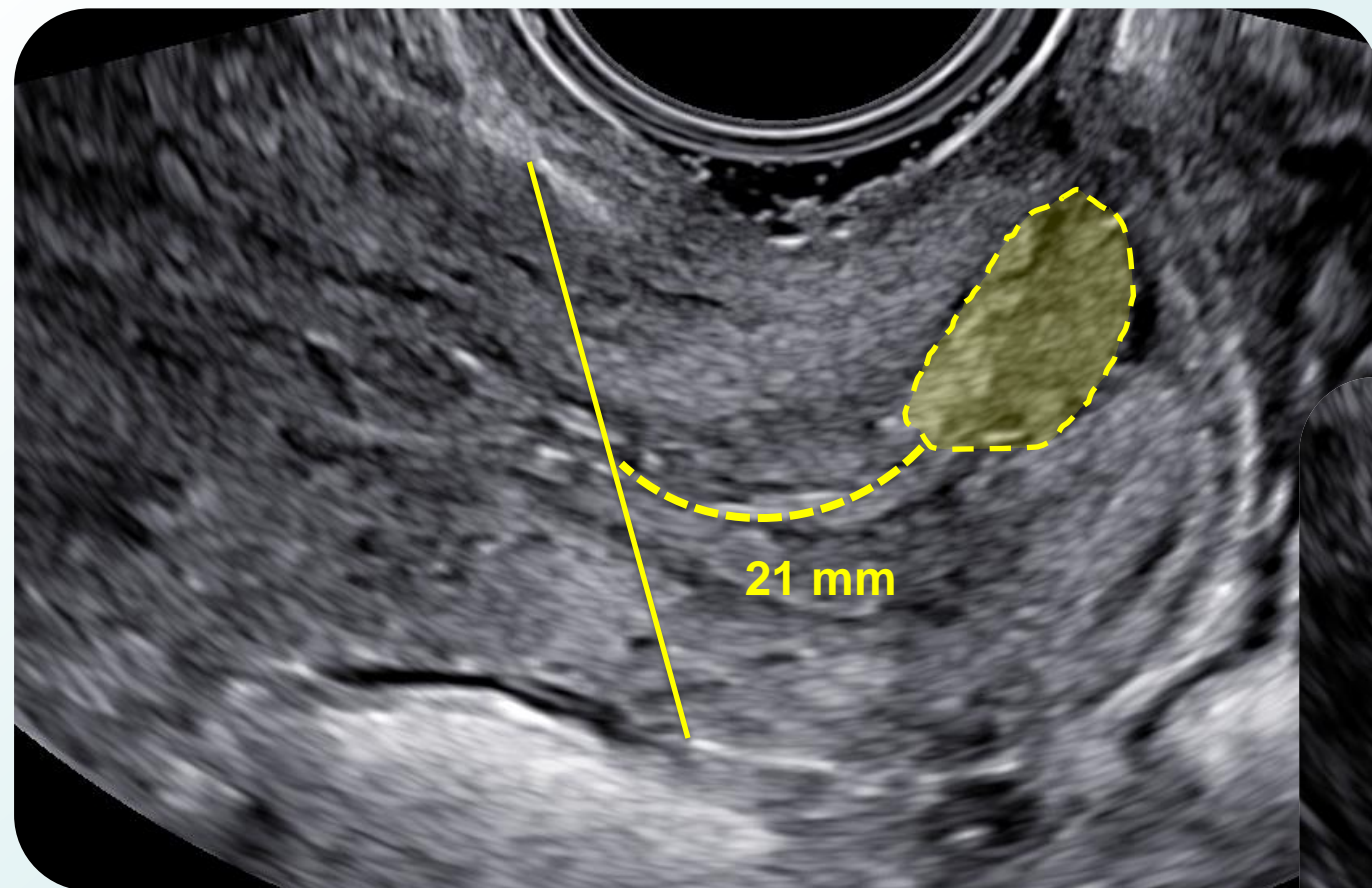
Inf stromale > 5 mm e diam max < 2 cm



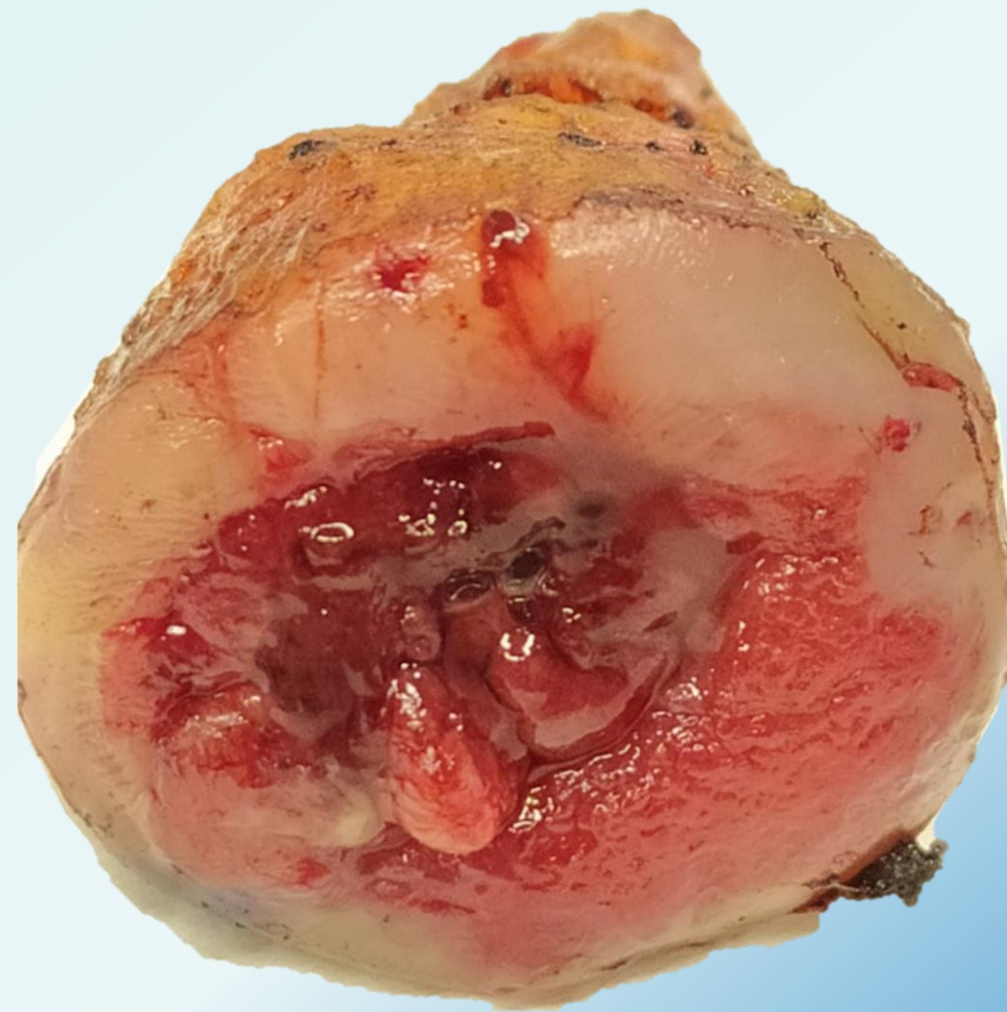
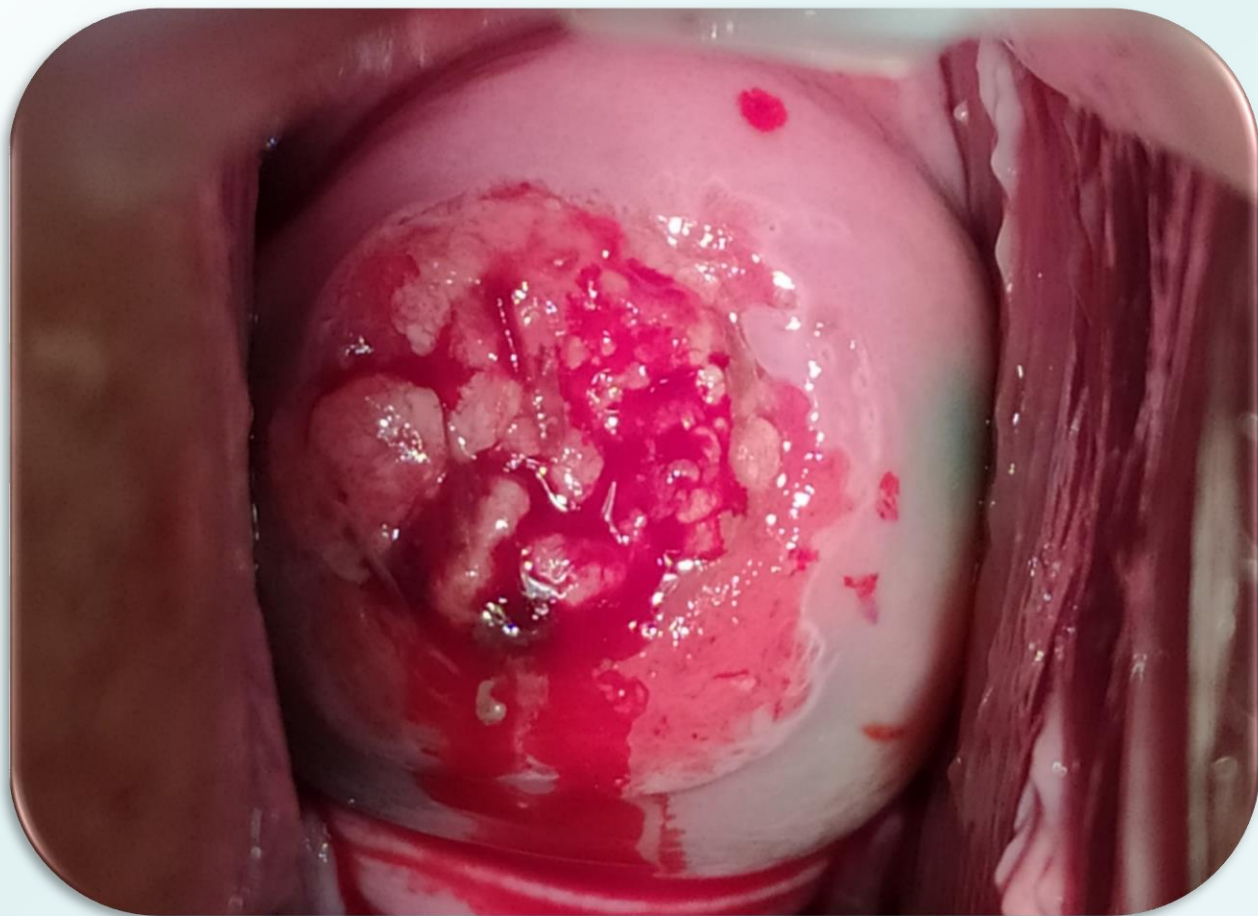
malattia residua: estensione > 7 mm infiltrazione > 3 mm  
STOP percorso conservativo







TVUS diameter 13x8x11 mm



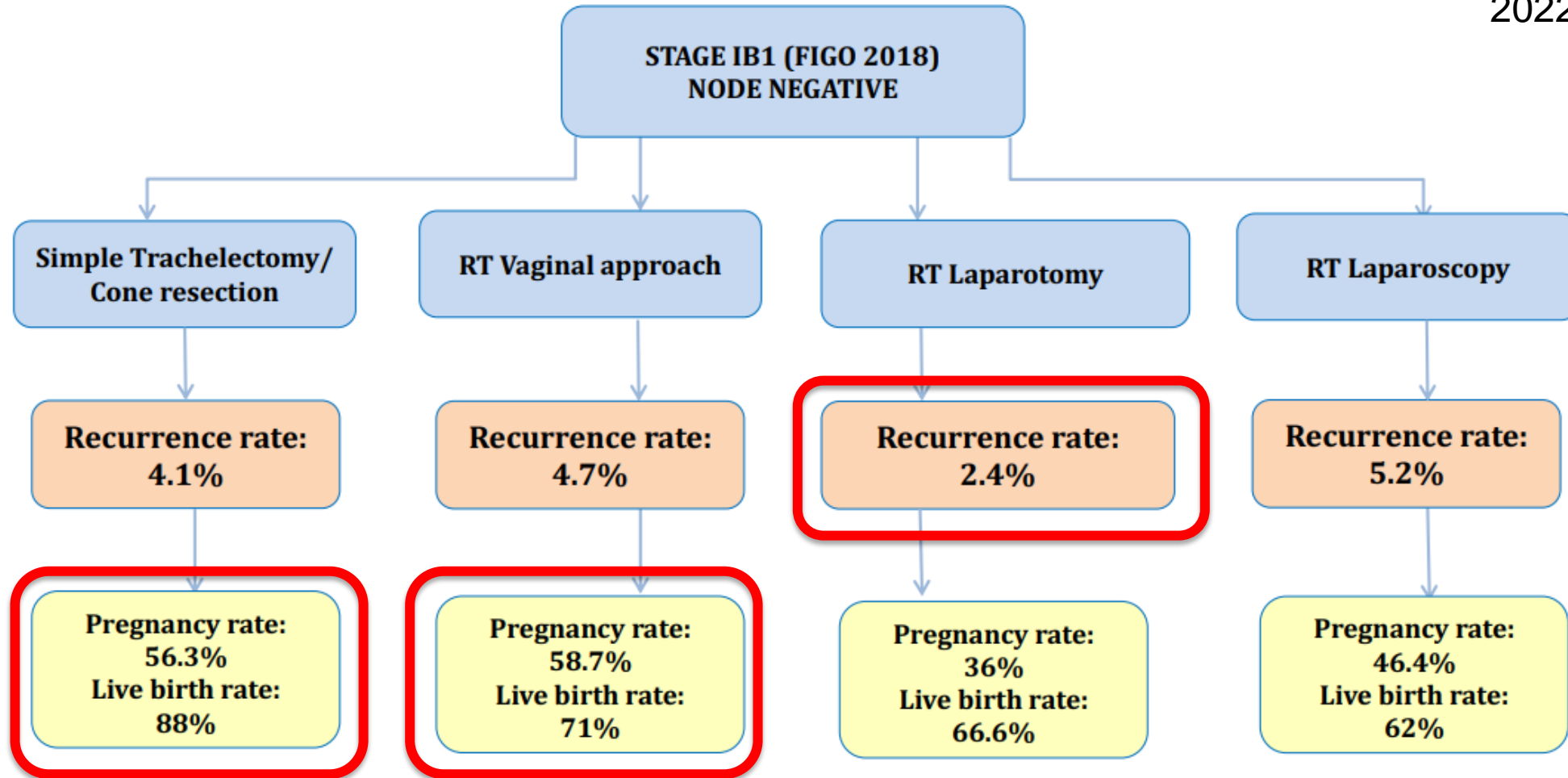
Final pathology: adenocarcinoma stage IB1 N-

# Oncologic results of fertility sparing surgery of cervical cancer: An updated systematic review



Morice Ph<sup>a,b,c,\*</sup>, A. Maulard<sup>a</sup>, S. Scherier<sup>a</sup>, C. Sanson<sup>a</sup>, J. Zarokian<sup>a</sup>, F. Zaccarini<sup>a</sup>, S. Espenel<sup>d</sup>, P. Pautier<sup>e</sup>, A. Leary<sup>e,f</sup>, C. Genestie<sup>g</sup>, C. Chargari<sup>b,d</sup>, M. Grynberg<sup>c,h</sup>, S. Gouy<sup>a</sup>

2022



# Neoadjuvant chemotherapy prior to fertility-sparing surgery in cervical tumors larger than 2 cm: a systematic review on fertility and oncologic outcomes

2021

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205 patients

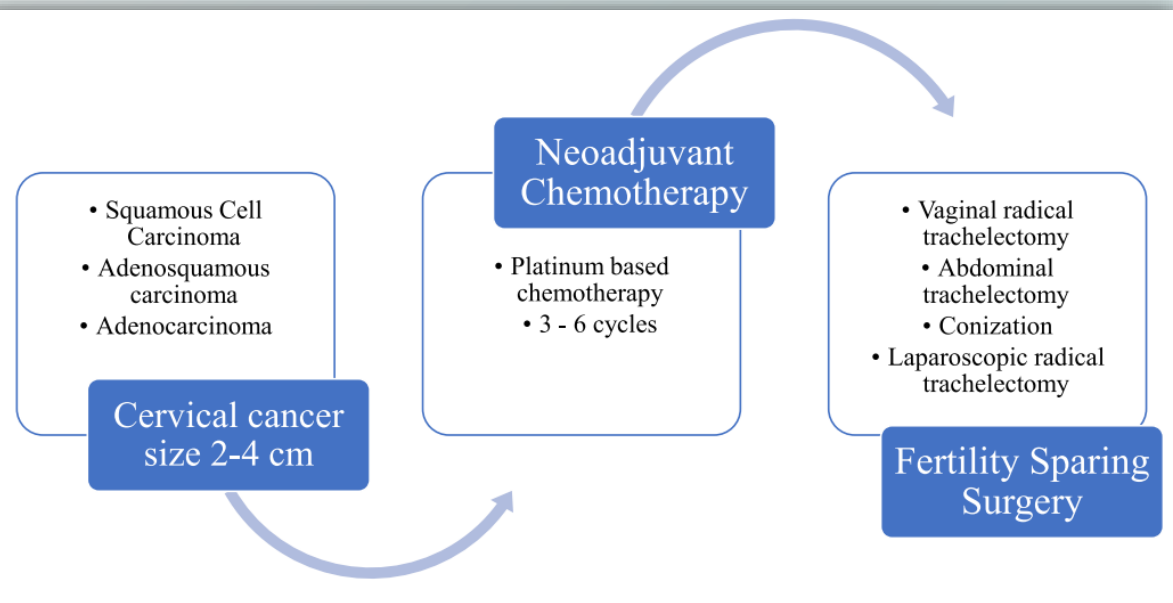
Review Article

# Neoadjuvant chemotherapy followed by fertility sparing surgery in cervical cancers size 2–4 cm; emerging data and future perspectives

114 patients

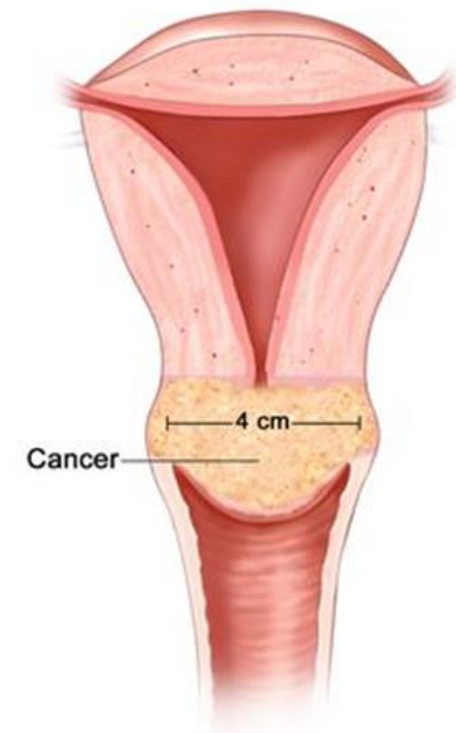
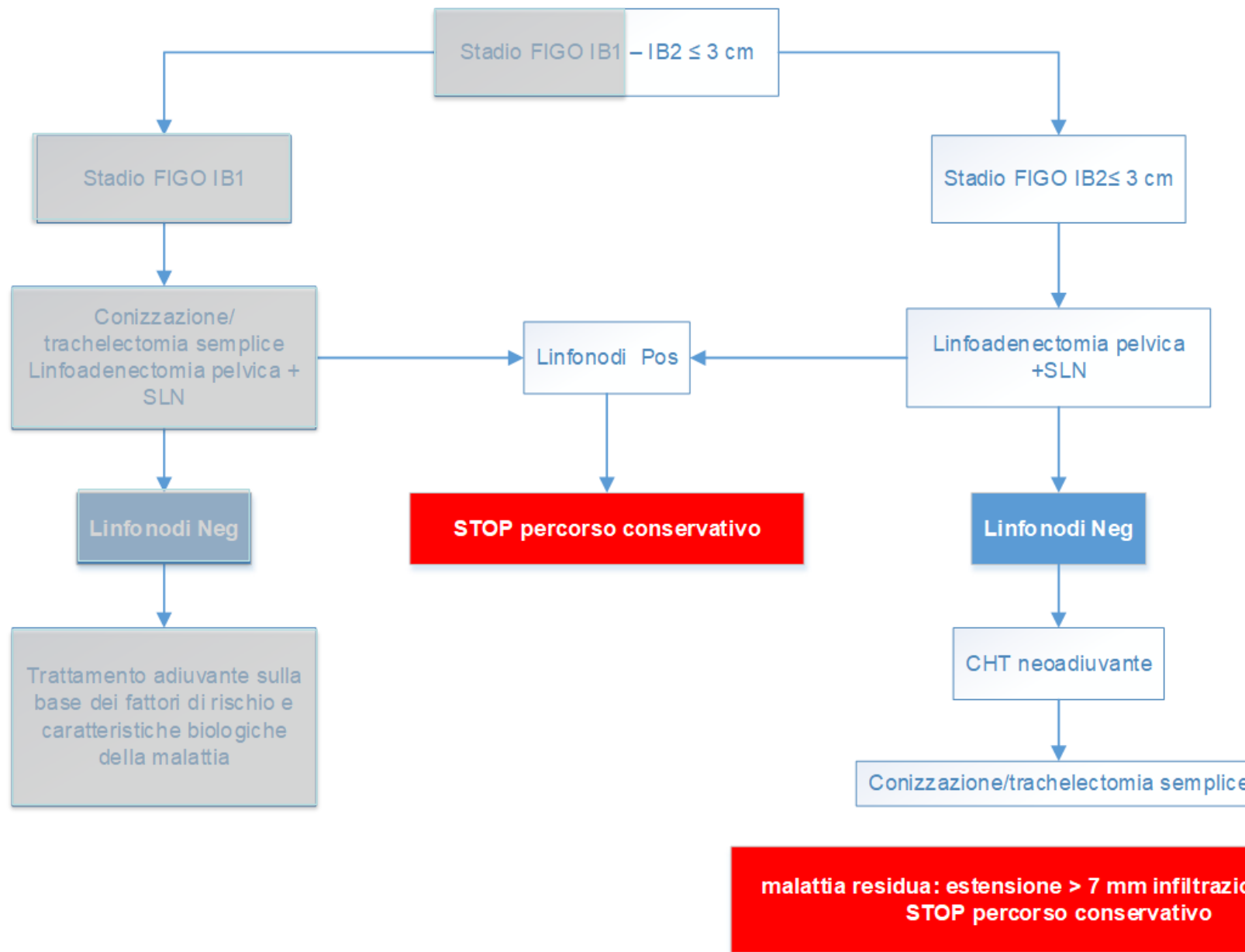
Nnamdi I. Gwacham <sup>a,\*</sup>, Nathalie D. McKenzie <sup>a,b</sup>, Evan R. Fitzgerald <sup>b</sup>, Sarfraz Ahmad <sup>a,b,\*</sup>, Robert W. Holloway <sup>a,b</sup>

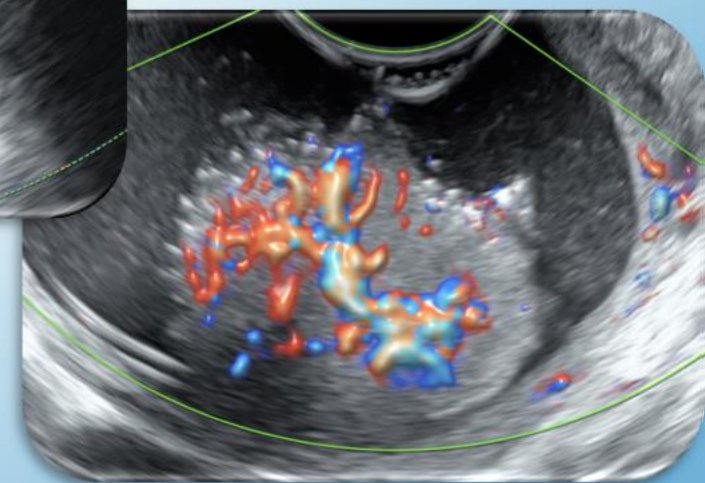
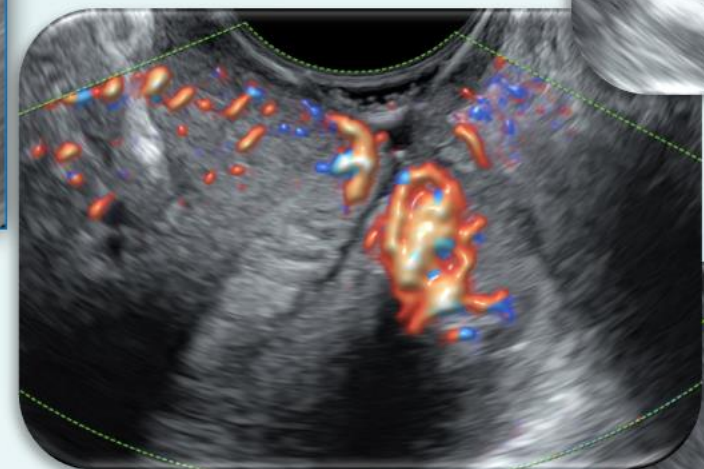
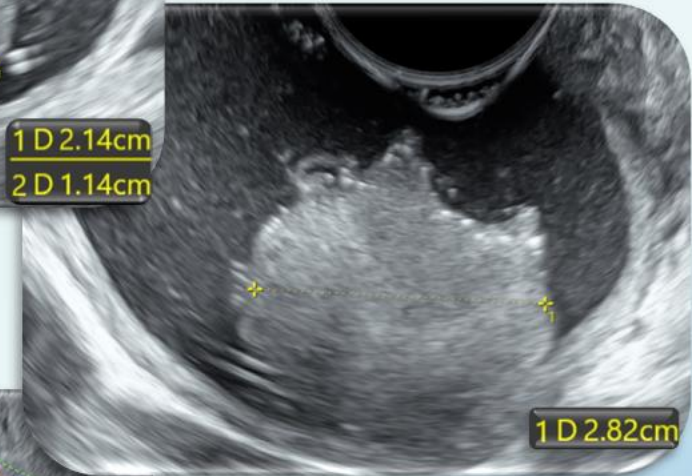
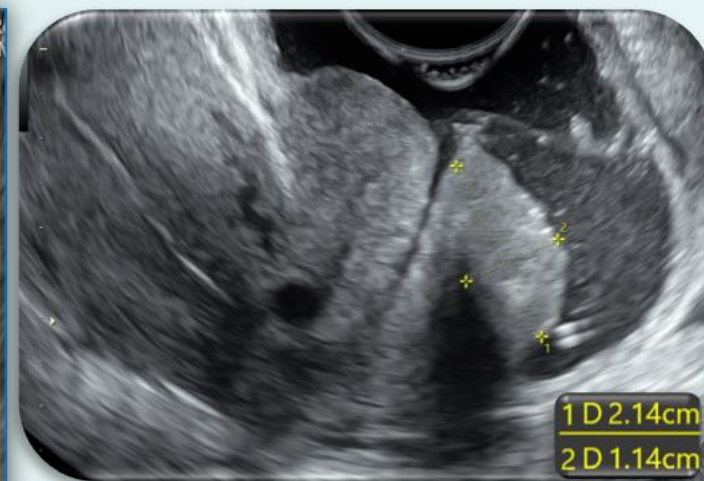
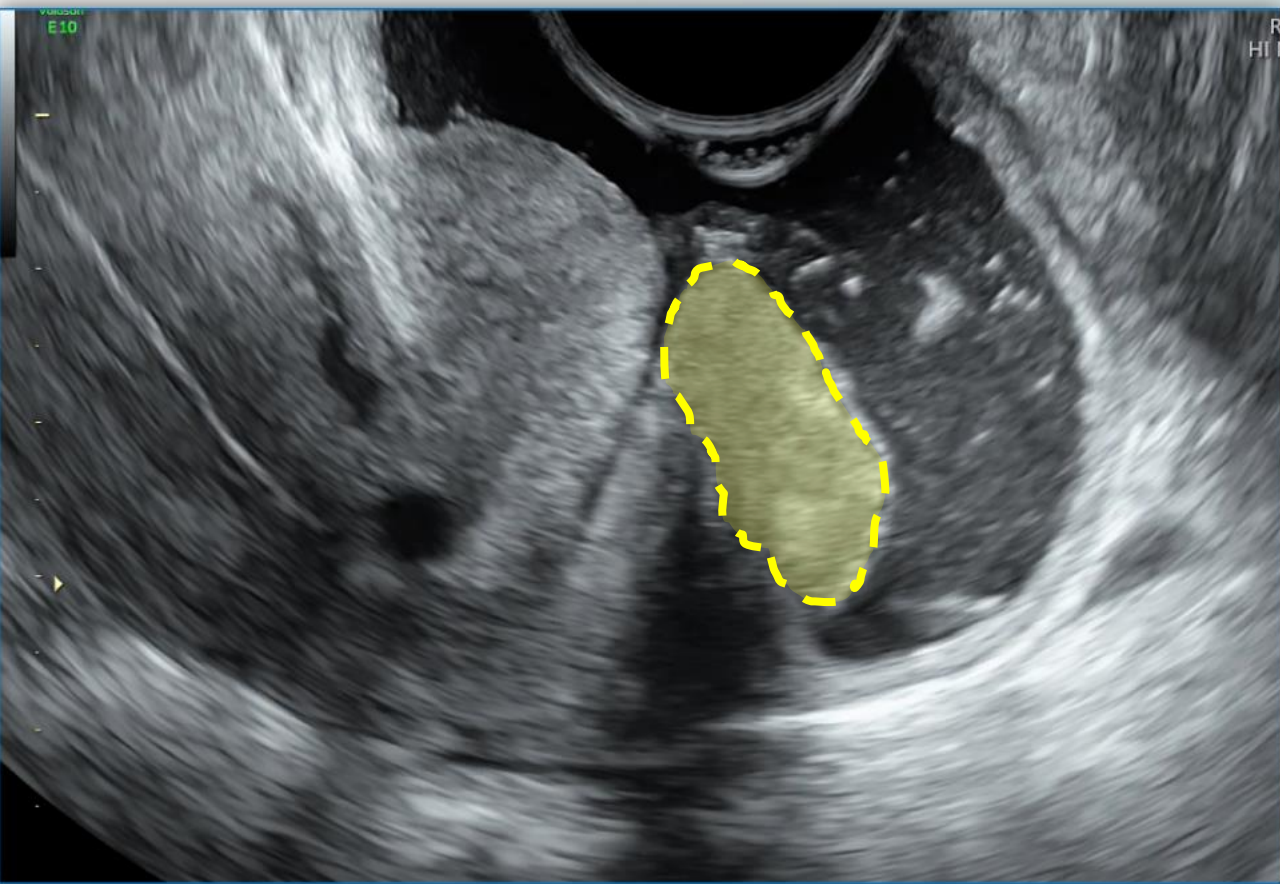
2021



- FST in tumors > 2 cm is considered as an experimental approach.
- The first selection criterion is node-negative disease
- Response rate 87-92%
- Relapse rate 6 - 12,8%
- Pregnancy rate 84 - 96%

**NACHT in cervical cancers 2– 4 cm prior to FSS: decrease tumor size, ease surgical resection, and reduced risk for postoperative adjuvant radiotherapy**





Age 34 yrs  
Squamous Cell Cancer  
FIGO stage IB2

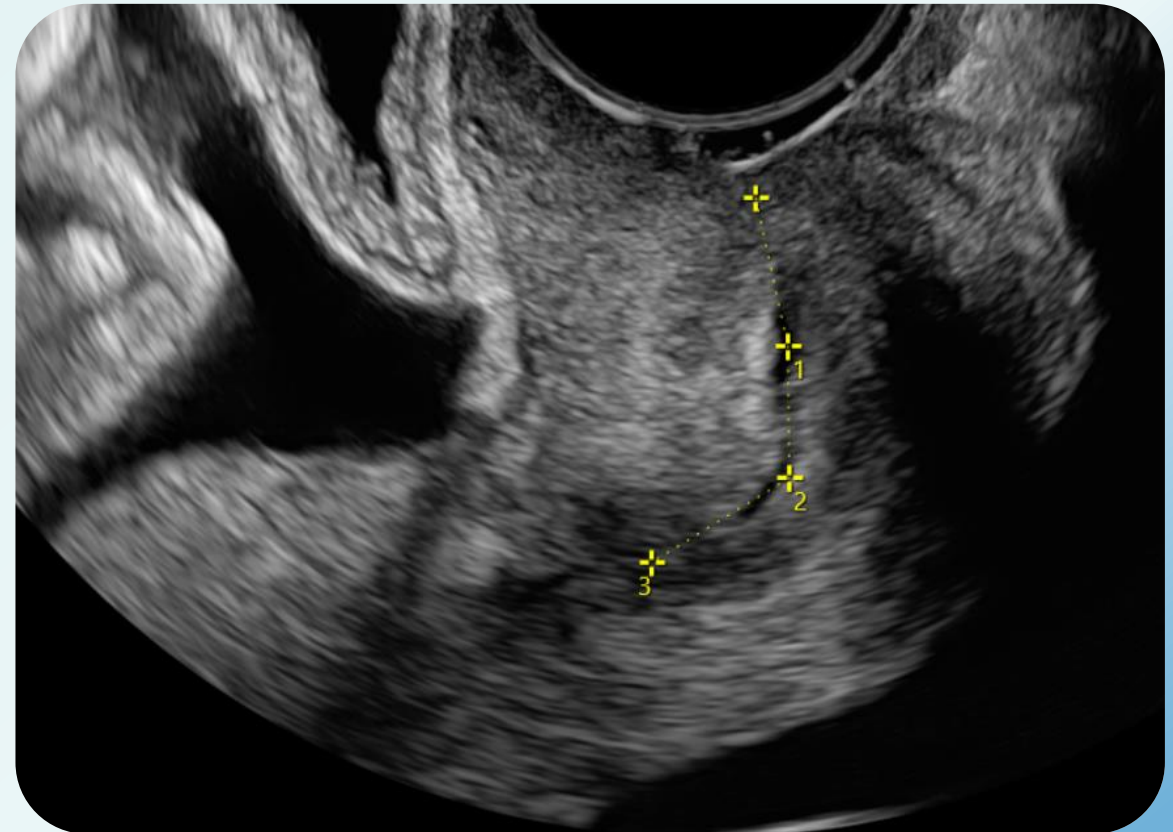
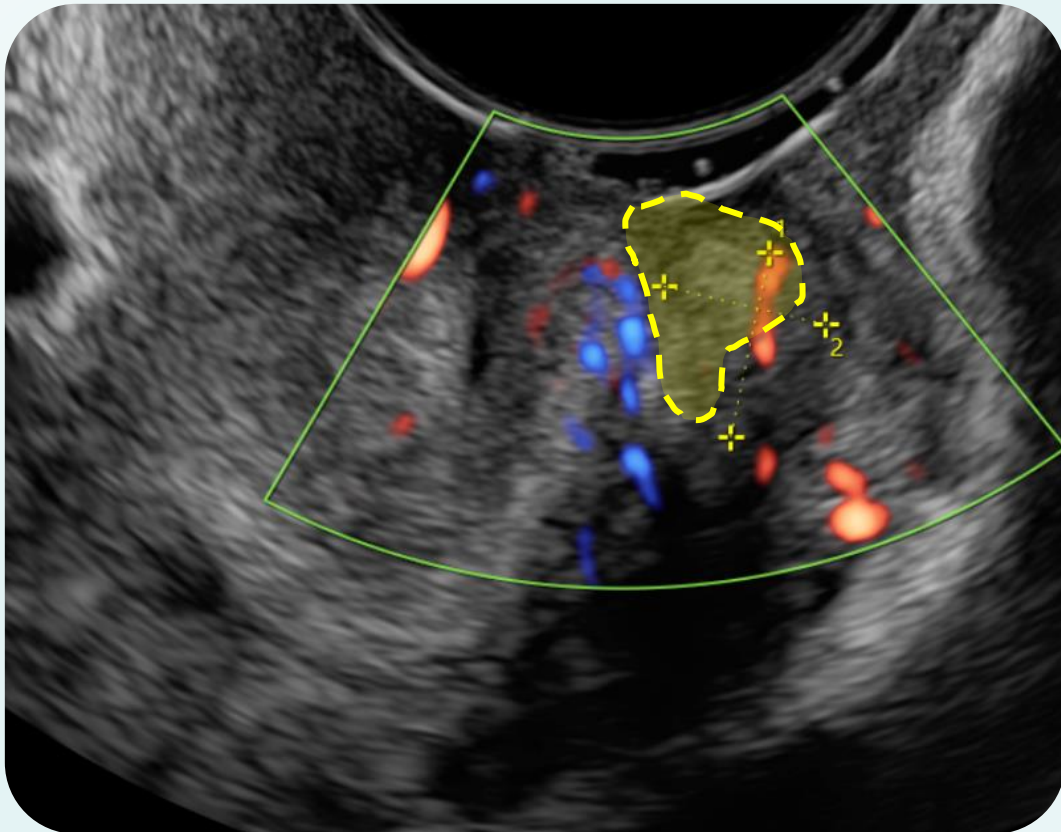
## Lymphadenectomy + NACHT (6 courses)

### Lasercone:

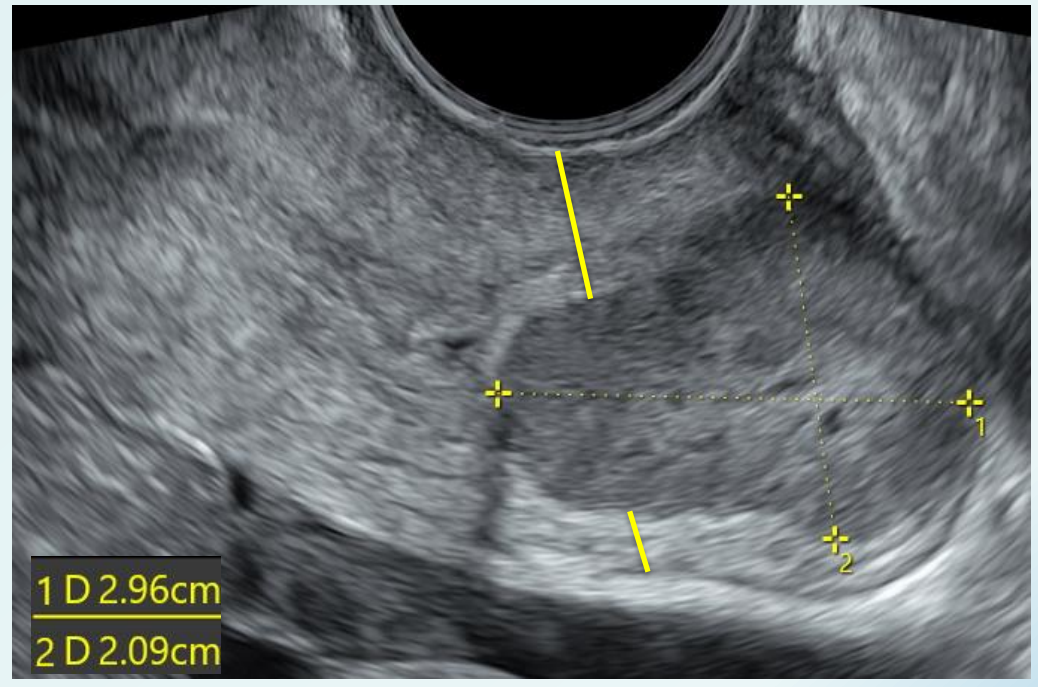
- residual tumor Max lenght 5 mm
- stromal infiltration 2,9 mm
- **free margin 0 mm**

## Further 3 Courses CHT

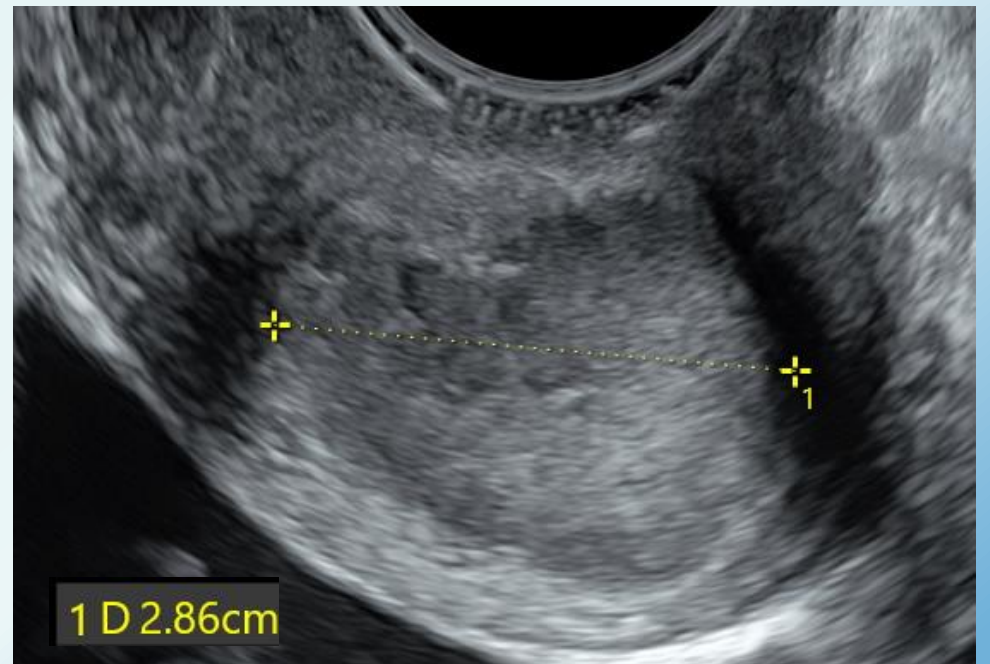
Lasercone: negative





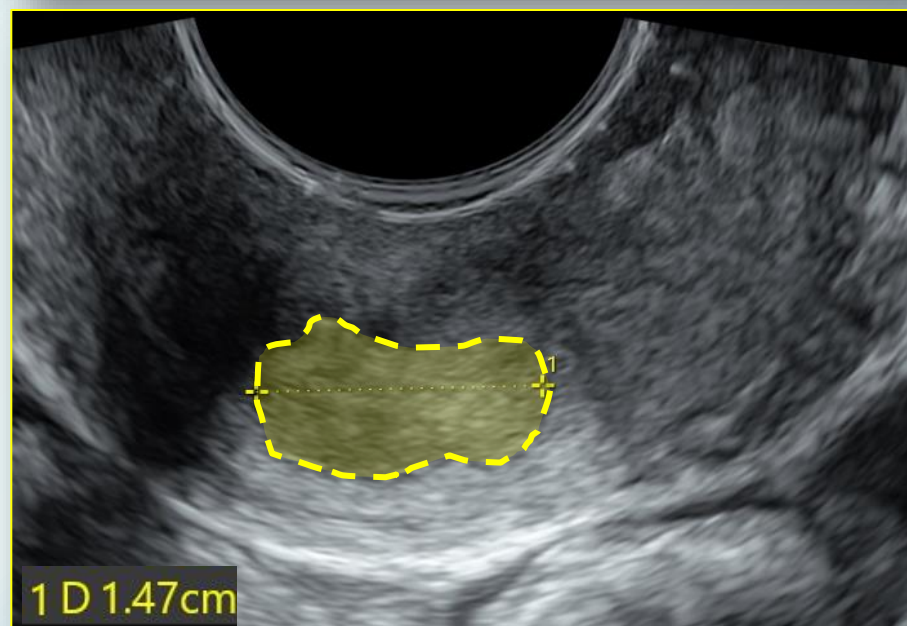
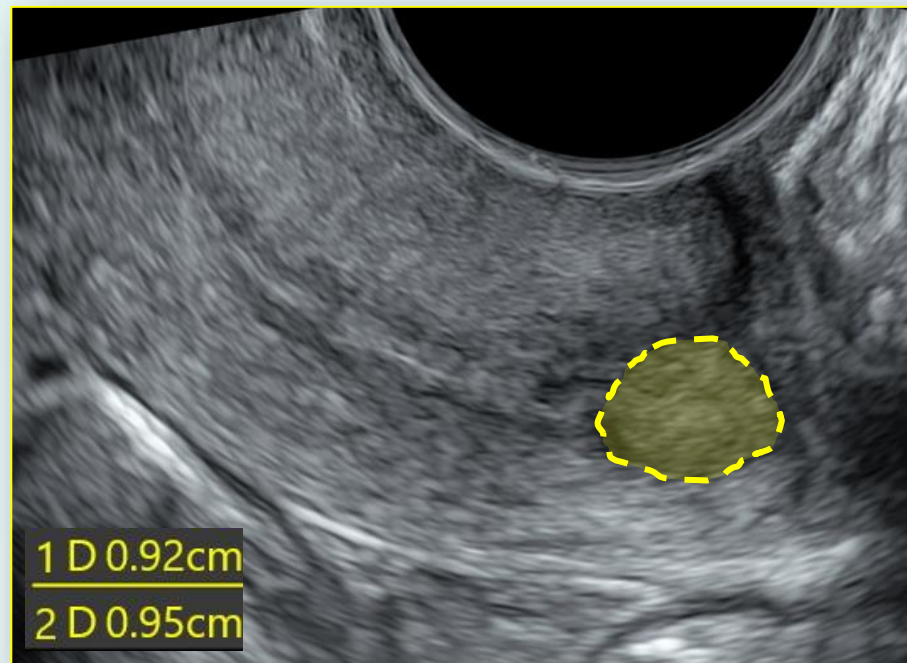


1 D 2.96cm  
2 D 2.09cm



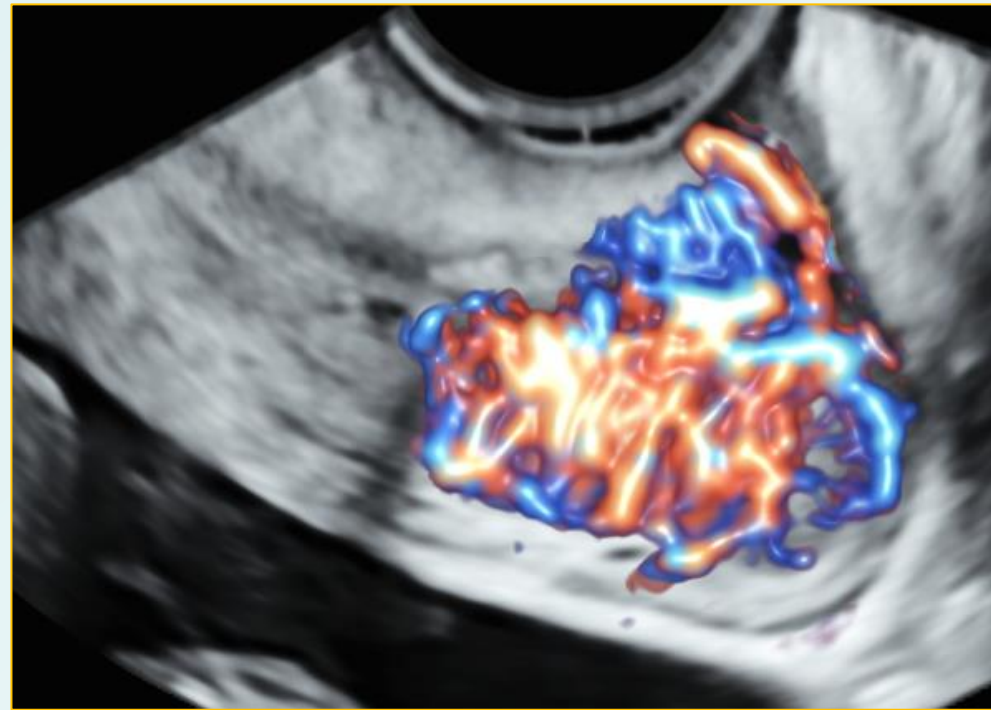
1 D 2.86cm

Age 33 yrs  
Squamous Cell Cancer  
FIGO stage IB2 N-

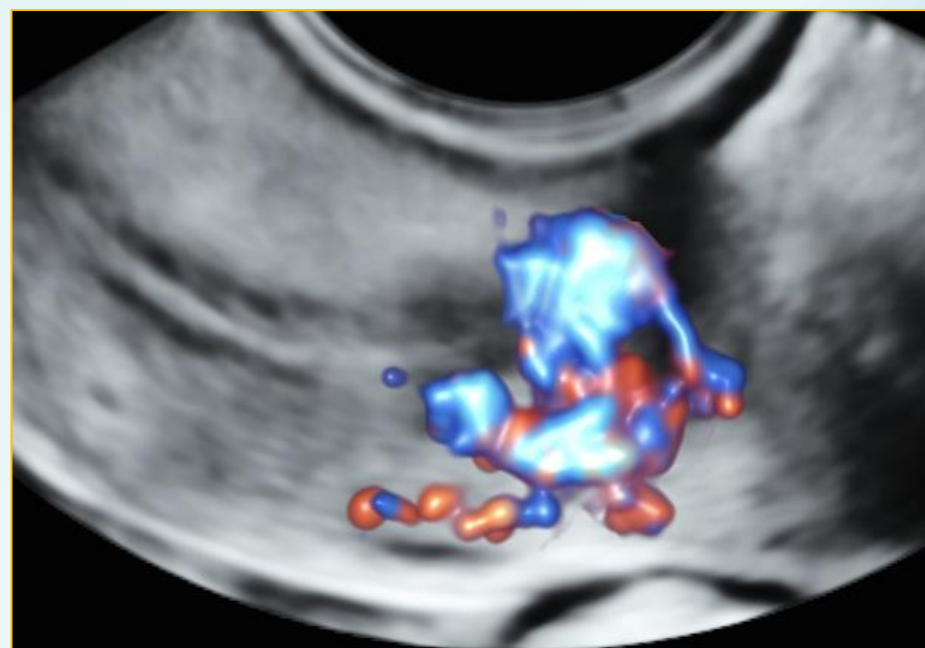


9 courses NACHT dose dense

Pre NACHT



Post NACHT



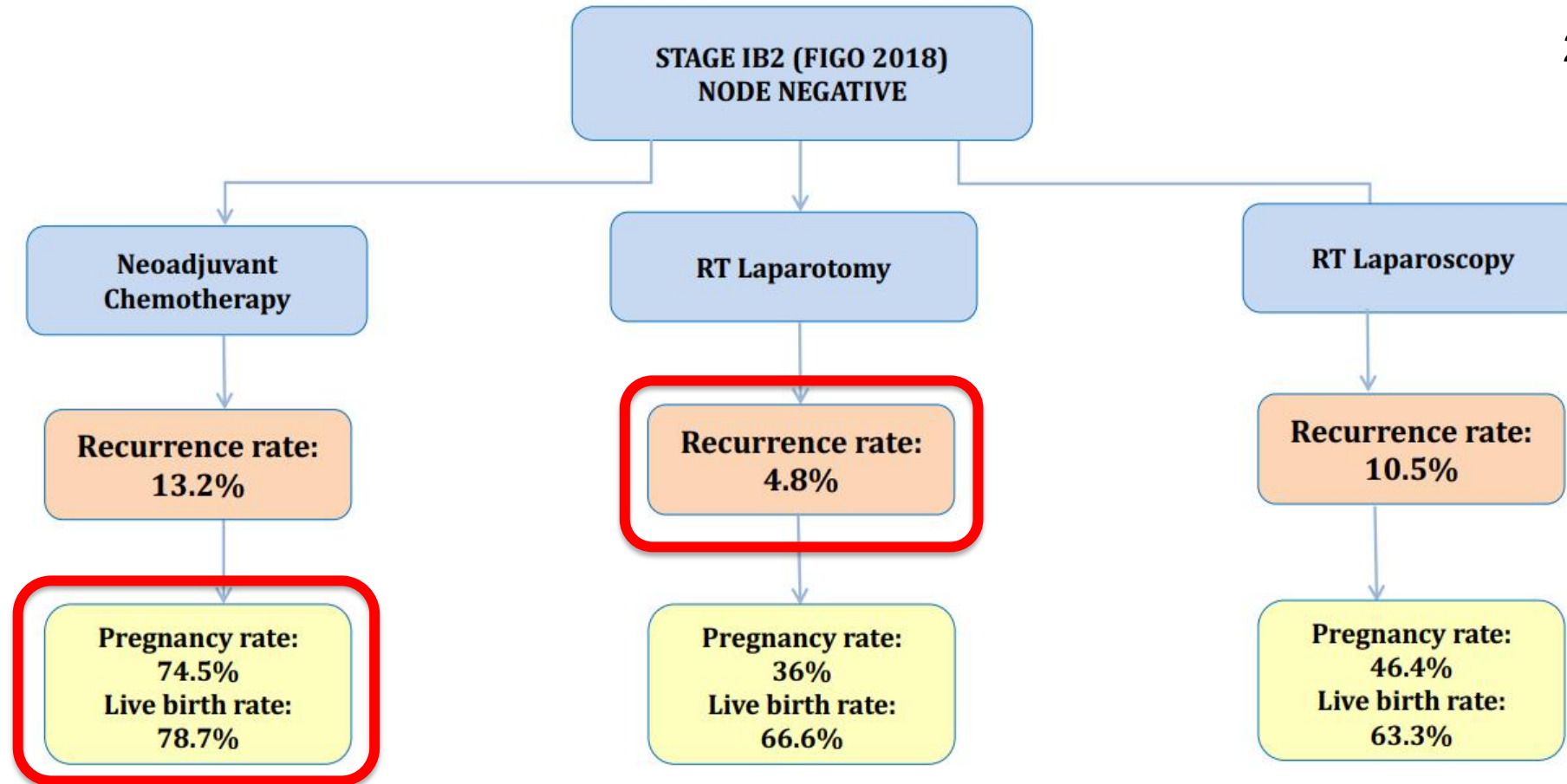
Final: y1b1  
16x12 mm

# Oncologic results of fertility sparing surgery of cervical cancer: An updated systematic review



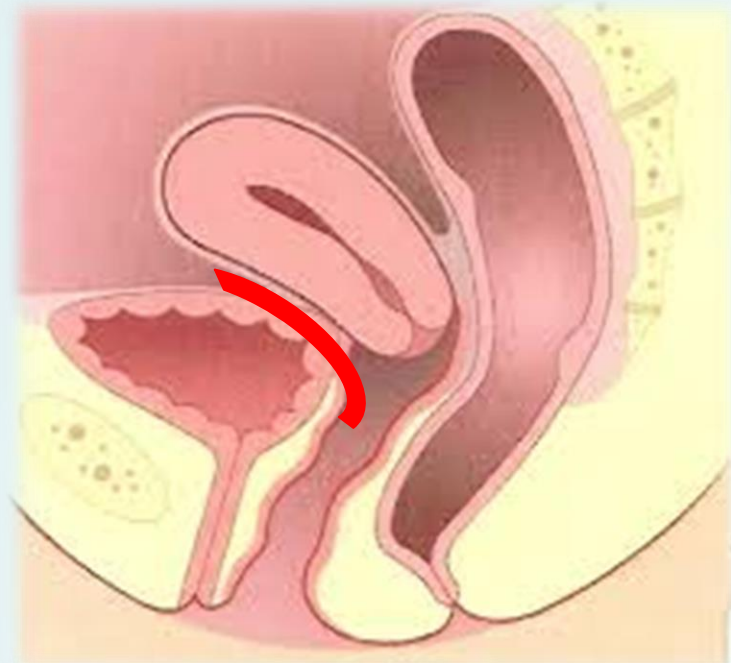
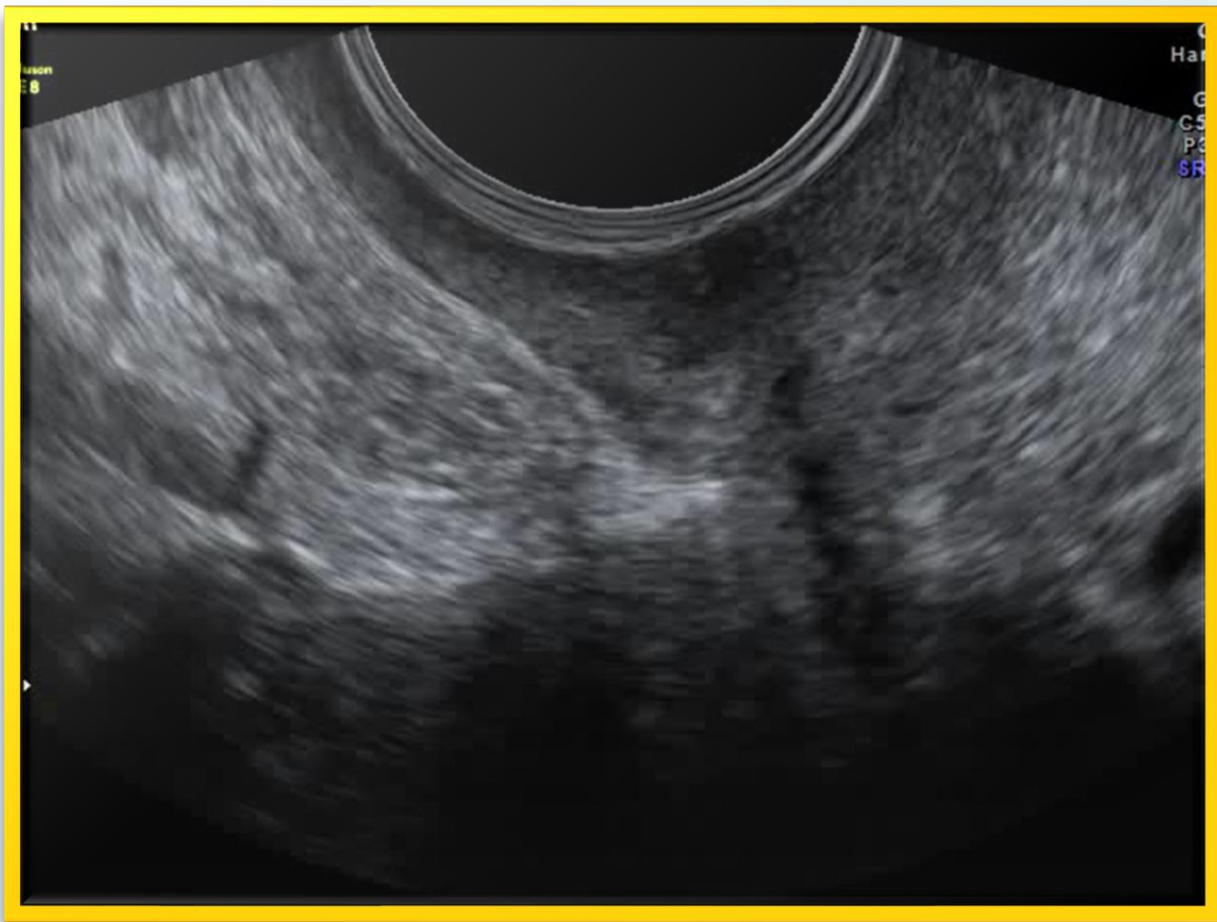
Morice Ph<sup>a,b,c,\*</sup>, A. Maulard<sup>a</sup>, S. Scherier<sup>a</sup>, C. Sanson<sup>a</sup>, J. Zarokian<sup>a</sup>, F. Zaccarini<sup>a</sup>, S. Espenel<sup>d</sup>, P. Pautier<sup>e</sup>,  
A. Leary<sup>e,f</sup>, C. Genestie<sup>g</sup>, C. Chargari<sup>b,d</sup>, M. Grynberg<sup>c,h</sup>, S. Gouy<sup>a</sup>

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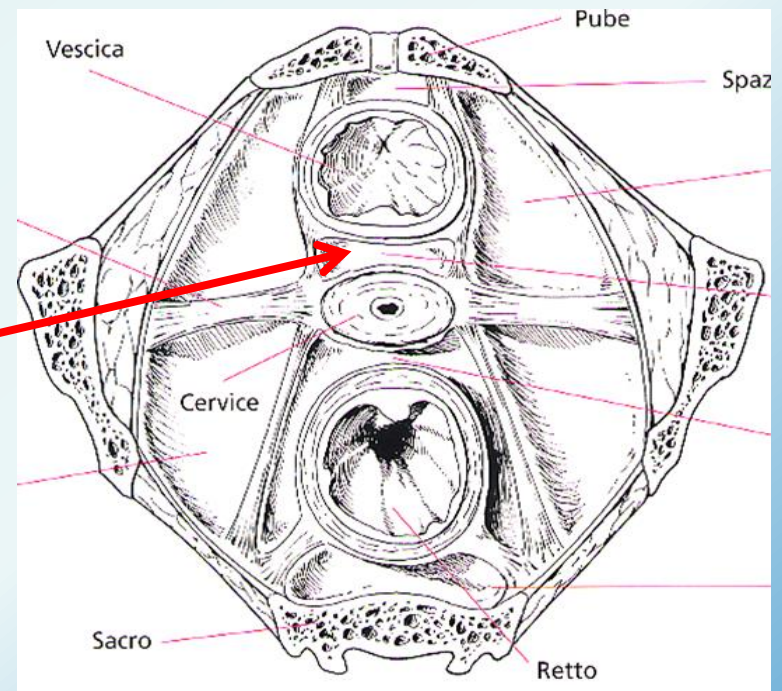
Don't forget a correct staging!

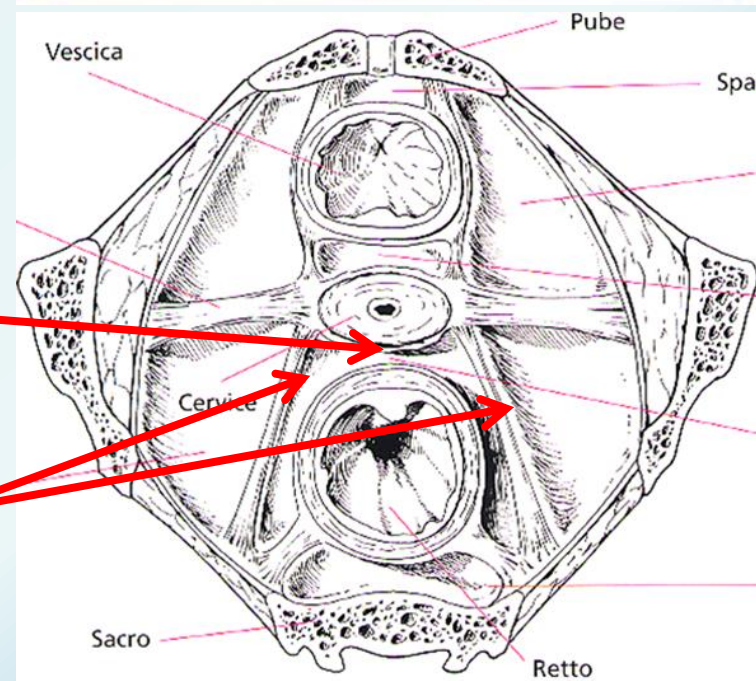
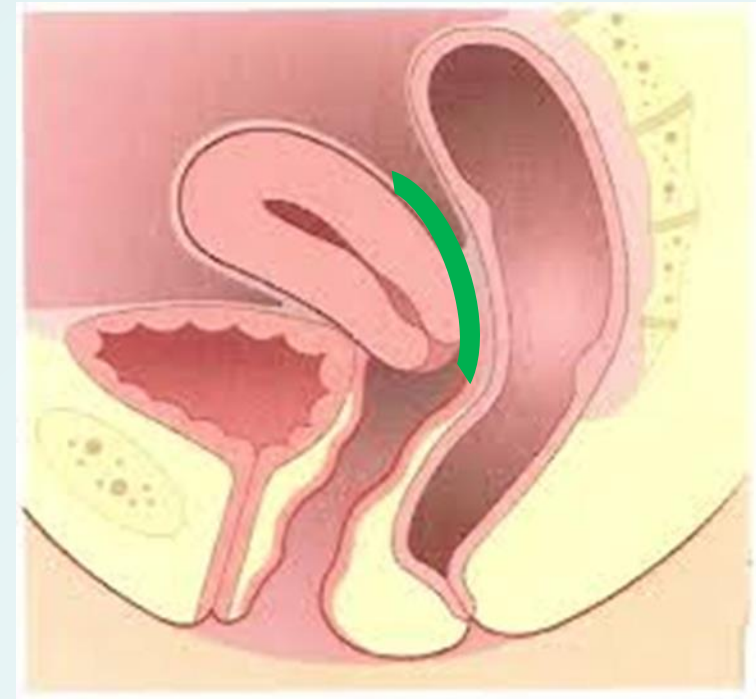
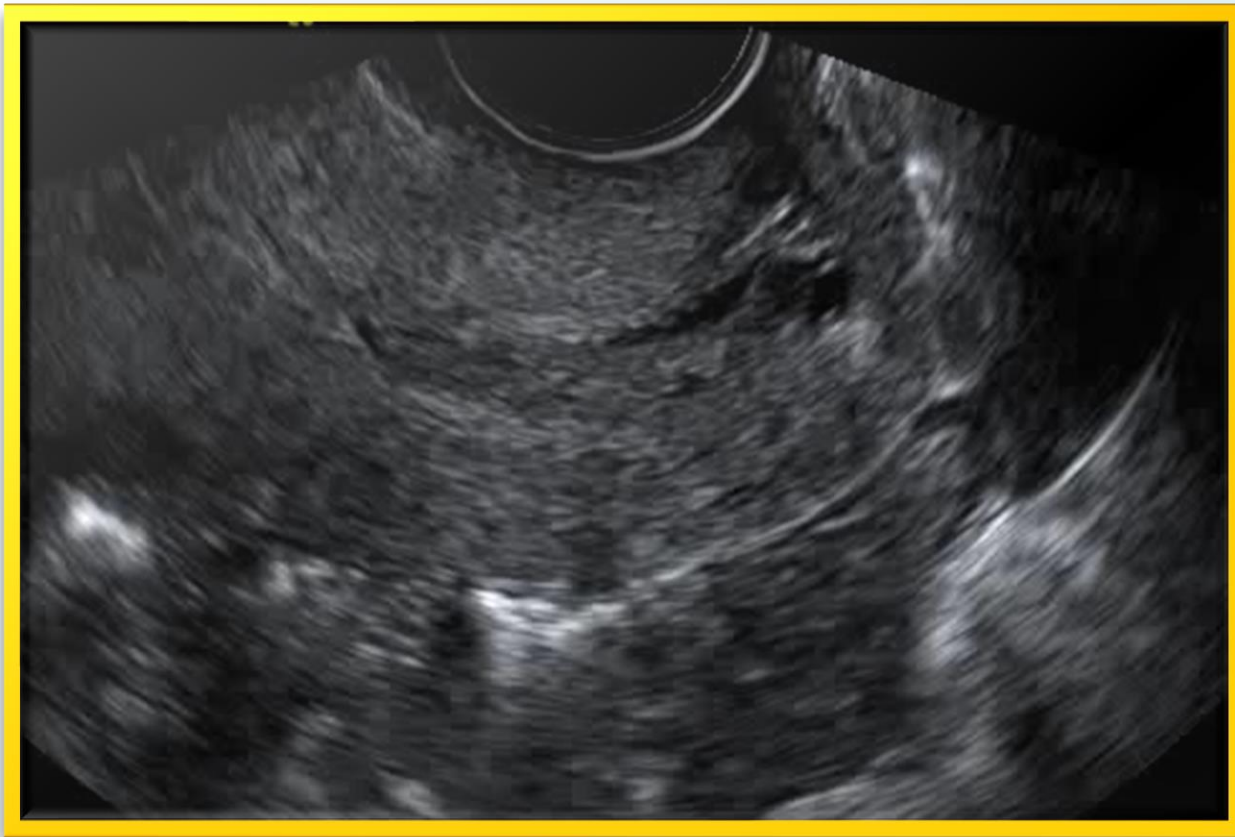




# Vescico-cervical space

## Anterior Compartment



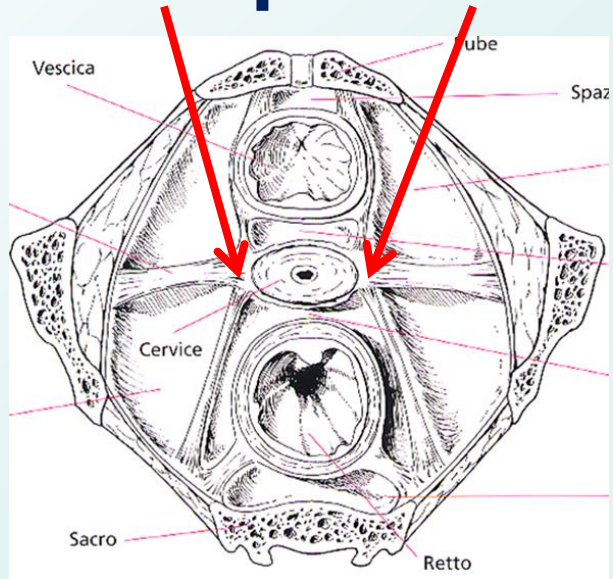


Recto-vaginal space

Utero-sacral ligaments

P  
O  
S  
T  
E  
R  
I  
O  
R  
  
C  
O  
M  
P  
A  
R  
T  
M  
E  
N  
T

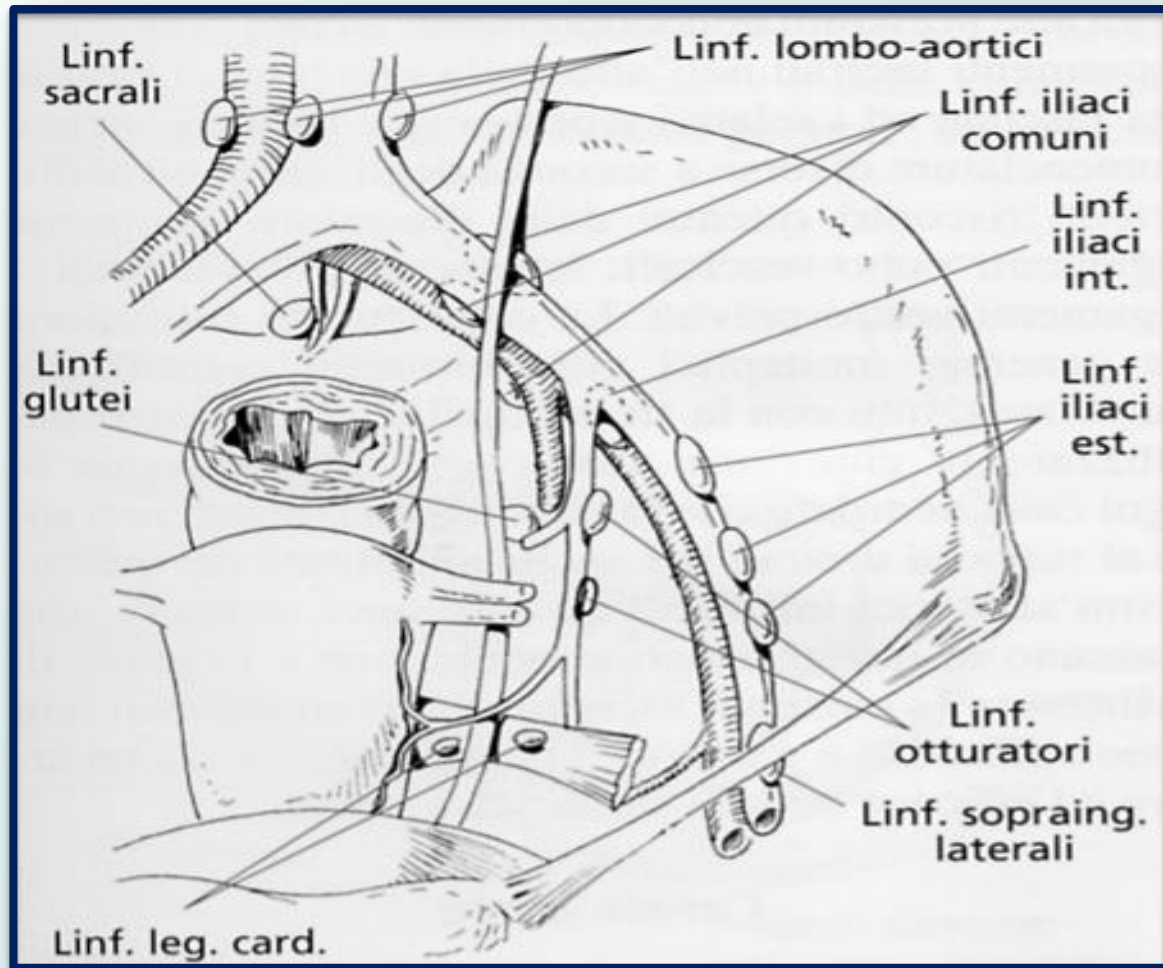
# Lateral parametria



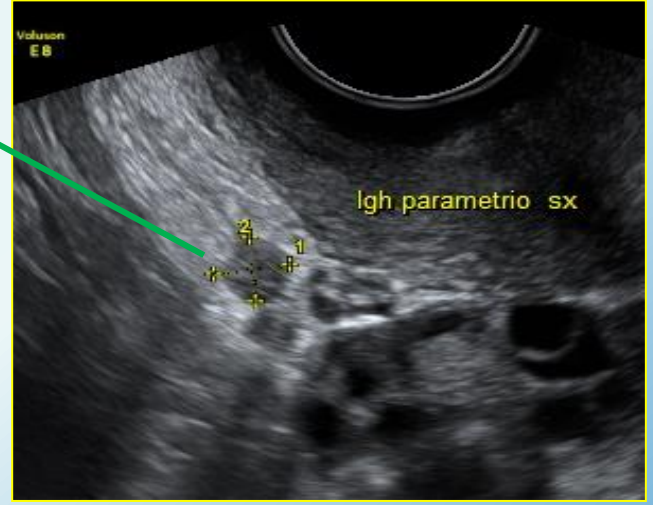
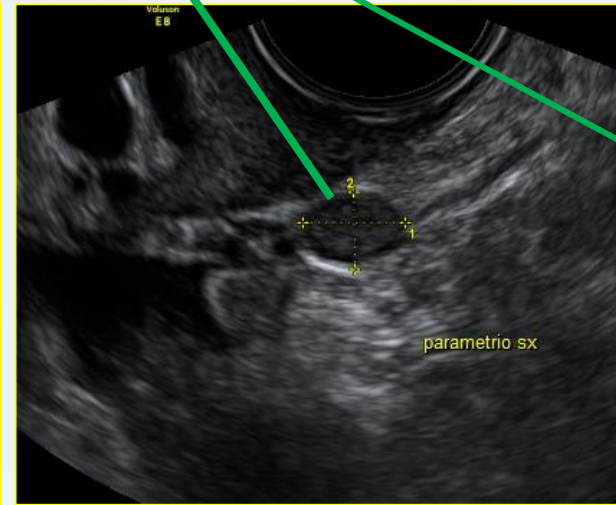
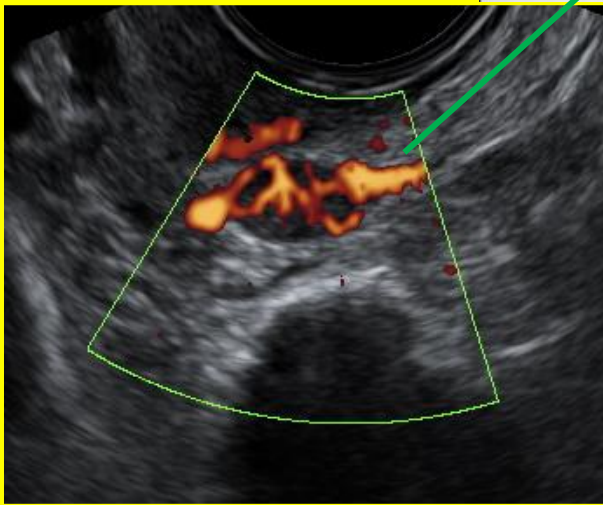
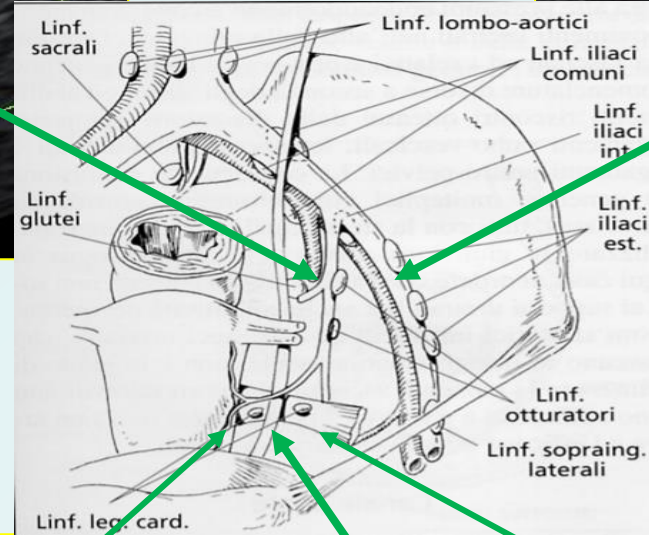
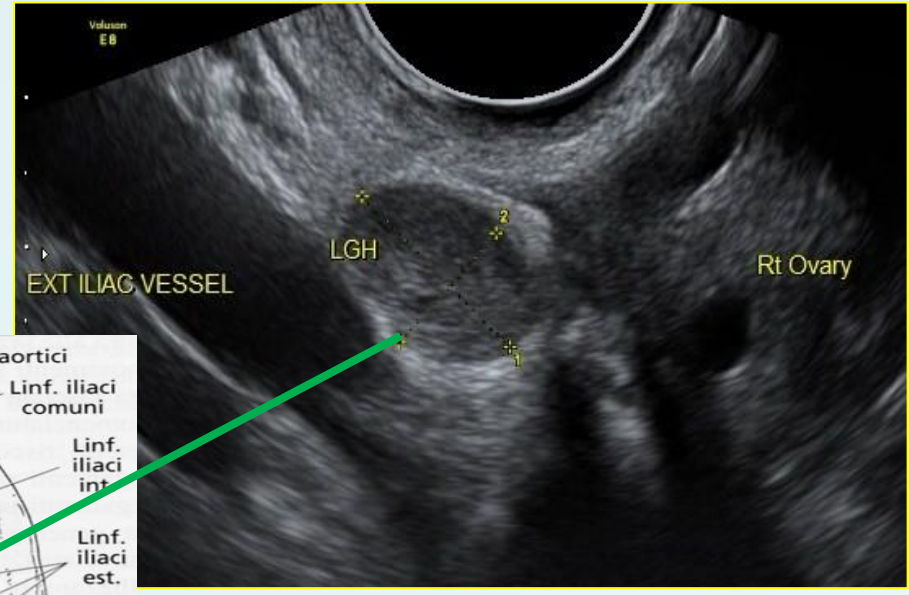
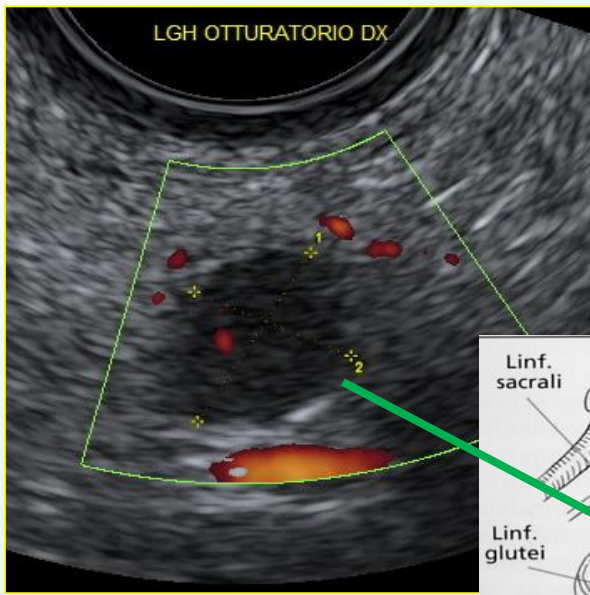


# Nodal Assessment

- Negative pelvic lymph node status is the **precondition for any FST**
- First step in each FST procedure: pelvic lymph node (sentinel lymph node) staging (and ultrastaging)
- In case of intraoperatively proven lymph node involvement, FST should be abandoned, and the patient referred to definitive chemoradiotherapy



**Can we use US to identify  
Pelvic Nodes?**





- ❖ Risk of tumor recurrence following FST
- ❖ Patients must be carefully followed up by expert gynecologic oncologist and colposcopist
- ❖ Follow-up intervals should be 3–4 months for the first 2 years postoperatively, and then 6 months up to 5 years.
- ❖ Pelvic MRI and TVUS once a year
- ❖ PET scan once a year (IA2 – IB1 - IB2 < 3 cm)
- ❖ Follow-up should include HPV testing (with or without cytology).
- ❖ Pregnancy is allowed after 12 months of negative controls
- ❖ Routine hysterectomy after finishing fertility plans is not mandatory (can be discussed according to clinical history)

# Conclusions

- In experienced hands ultrasound at least as good as MRI for the assessment of early cervical cancer
- The great advances in ultrasound technology
- Its relatively low cost
- The rapidity of the procedure
- The role of ultrasound in the pre-treatment work-up of cervical cancer in young patients must be considered

