Small diagnostic biopsies

Handling and reporting issues

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Newport

Biopsy vs. resection specimens

Smaller Tissues: Larger Issues

Biopsy pathology

Differences from resection pathology

Smaller Tissues: Larger Issues

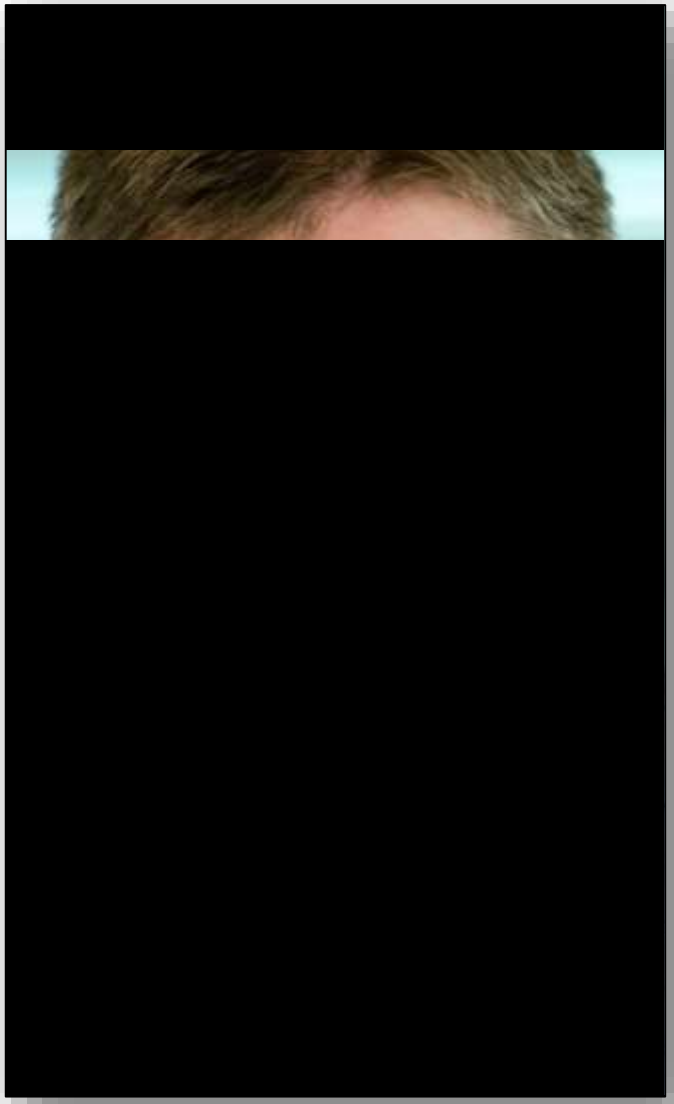
- **Interpretation** issues
- **Sampling** issues
- **Handling** issues
- **Time** constraints
- **Clinical** implications

Small biopsies

Interpretation issues

- Limited material
- Fragmented material
- Uncertain topography
- Background

Who is this?



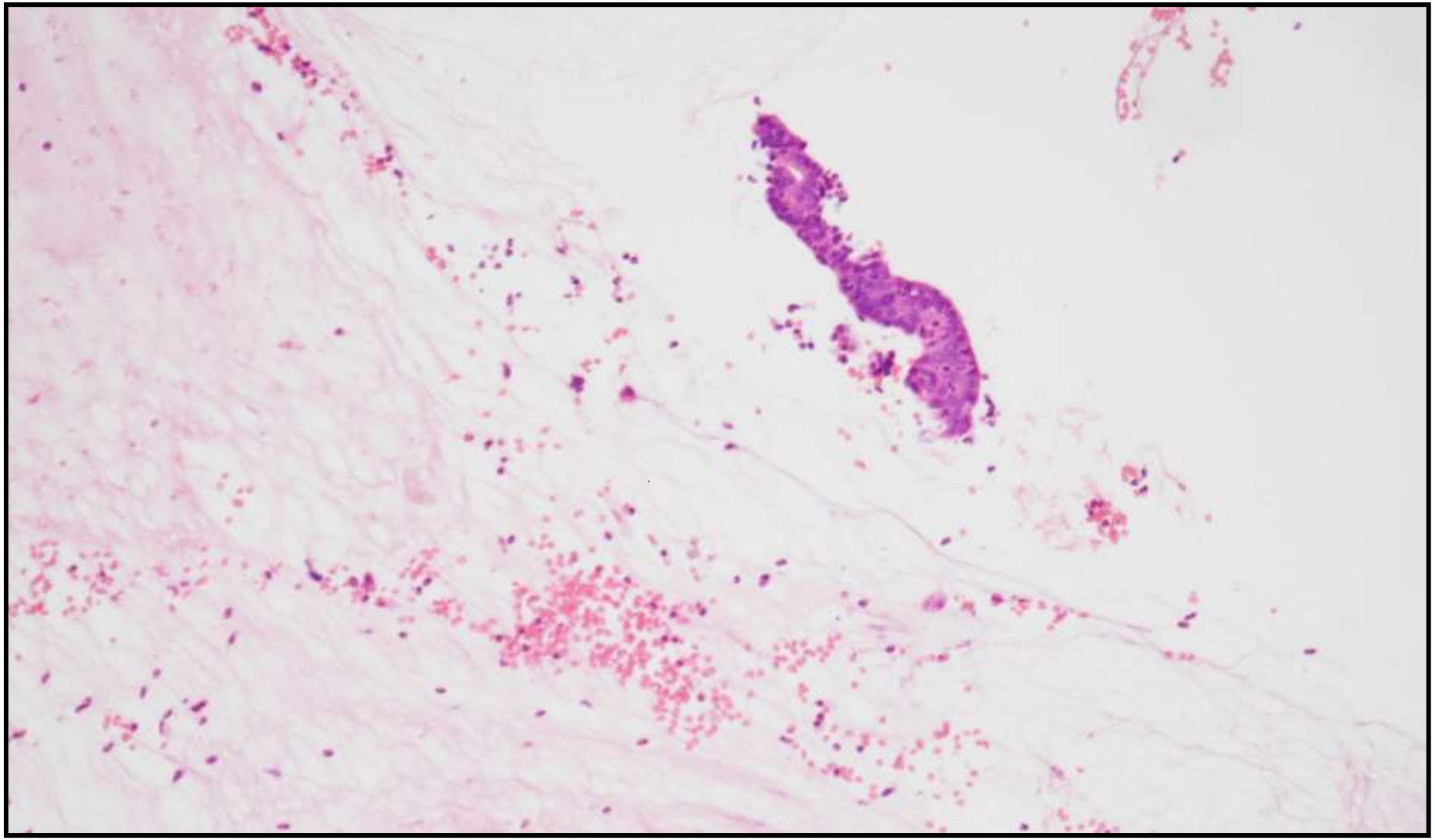
Who is this?

Who is this?

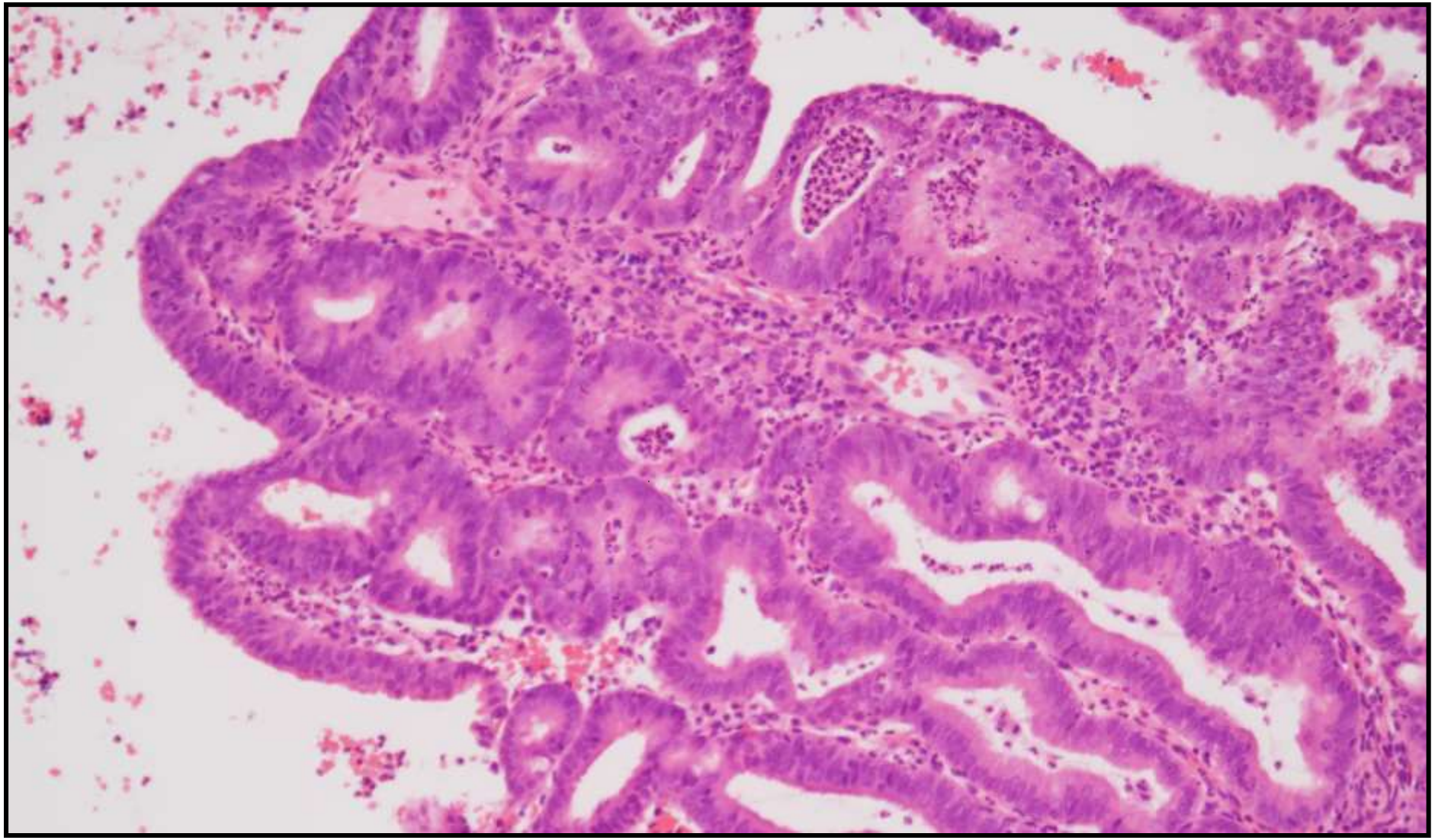
Interpretation issue

- **Very familiar obvious diagnosis difficult on limited material**

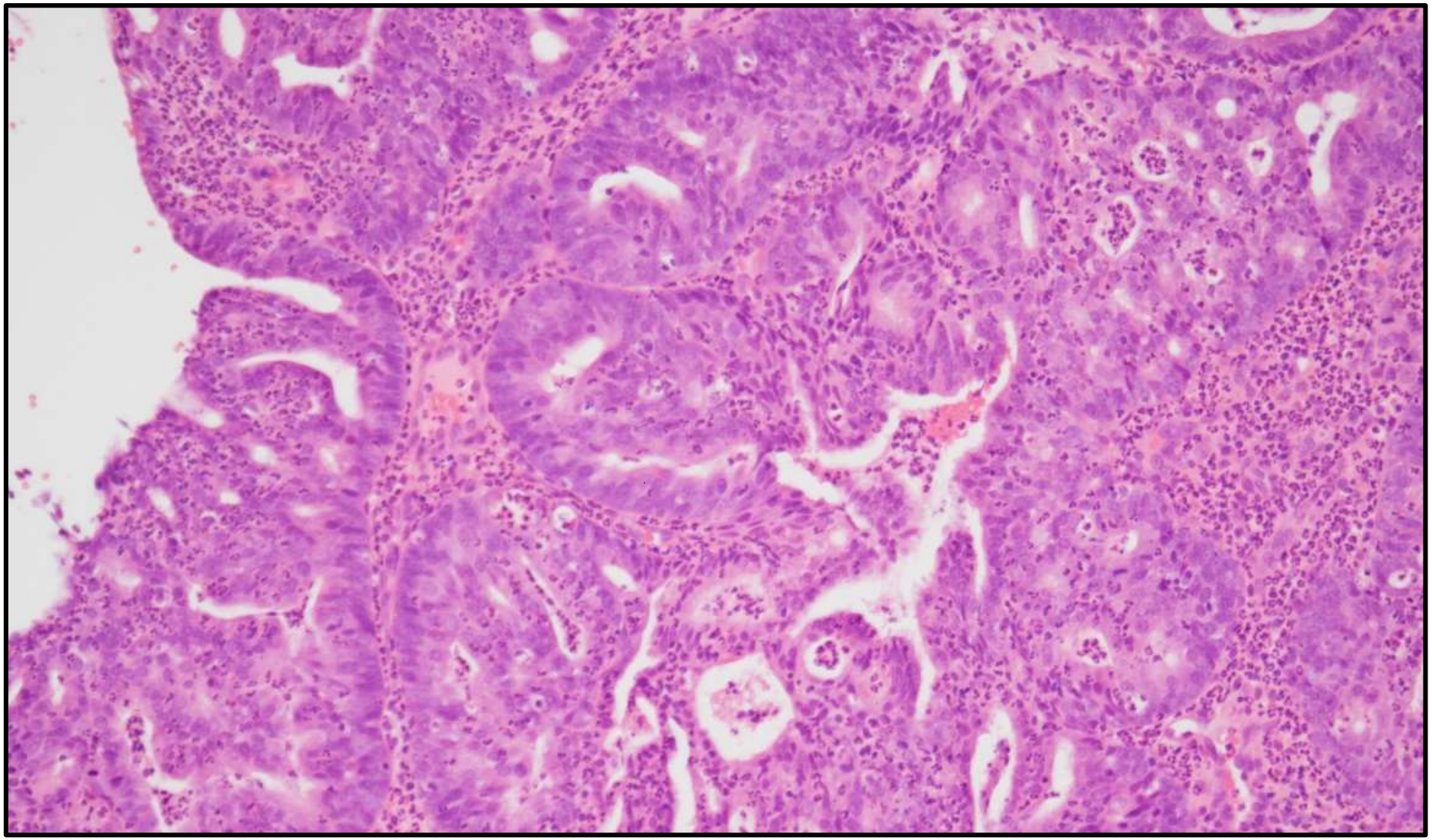
Endometrial bx



Endometrial bx



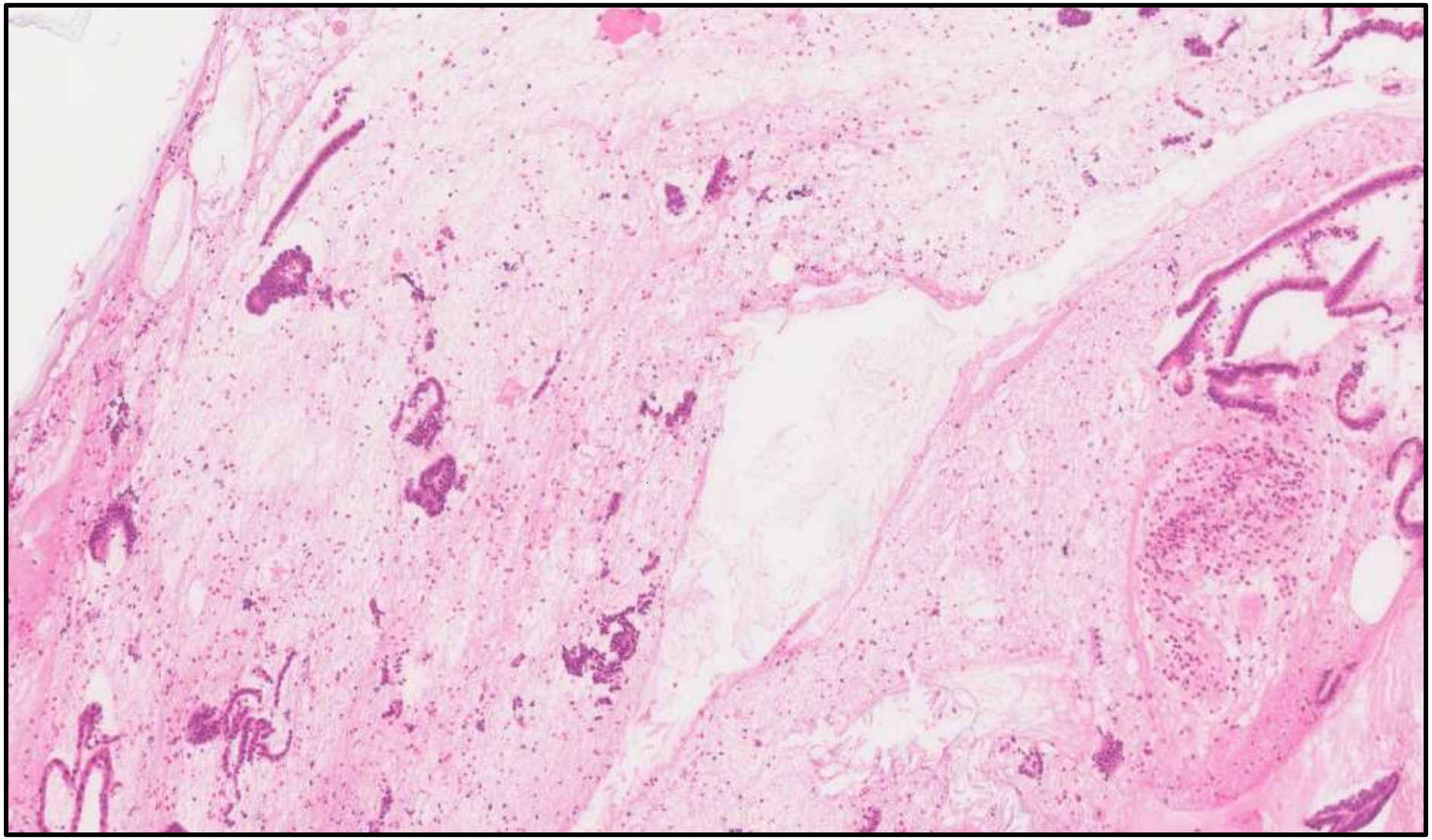
Endometrioid adenocarcinoma



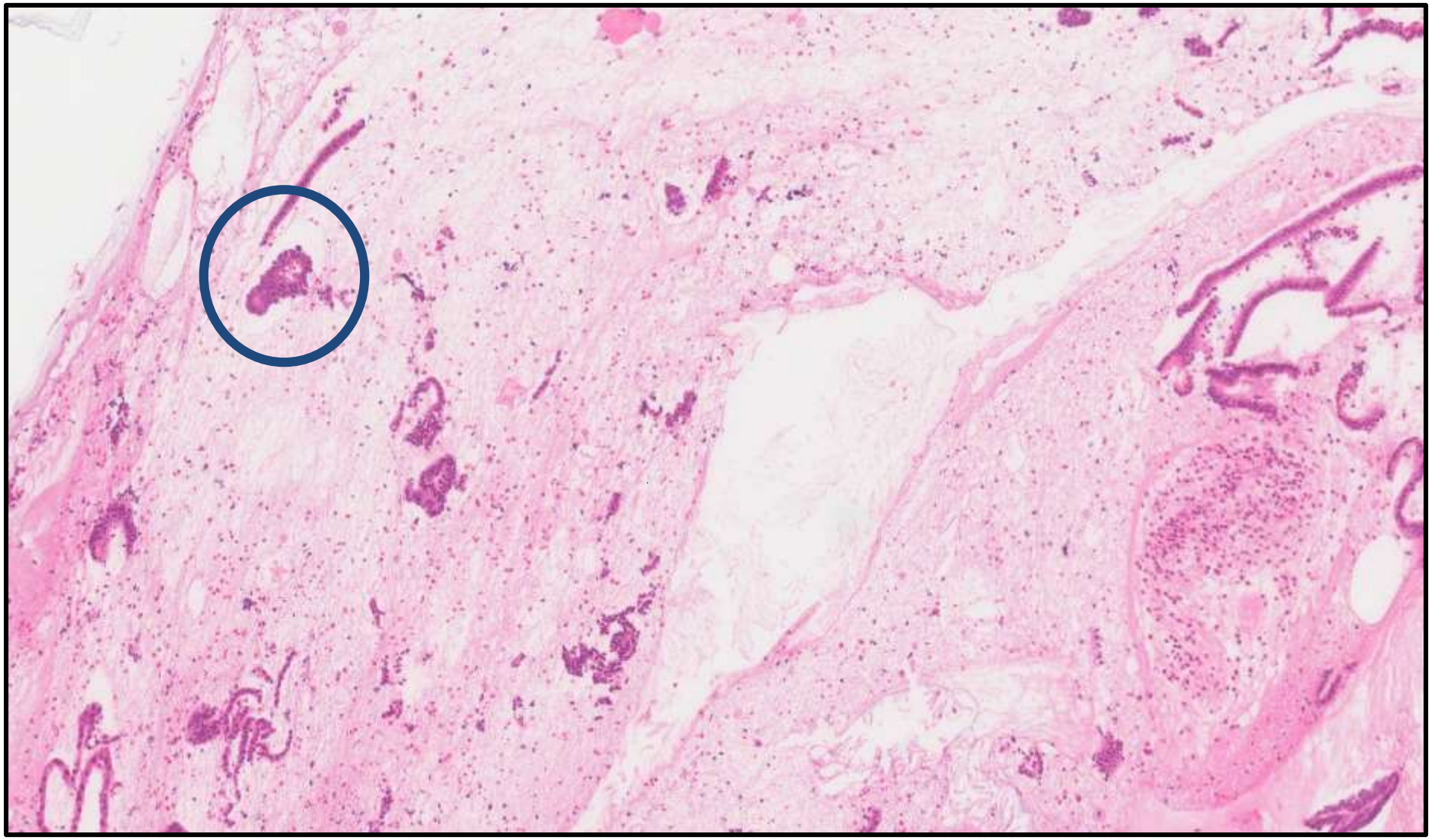
Interpretation issue

- **Very familiar obvious diagnosis difficult on limited material**
  - However, sometimes even limited material may be diagnostic

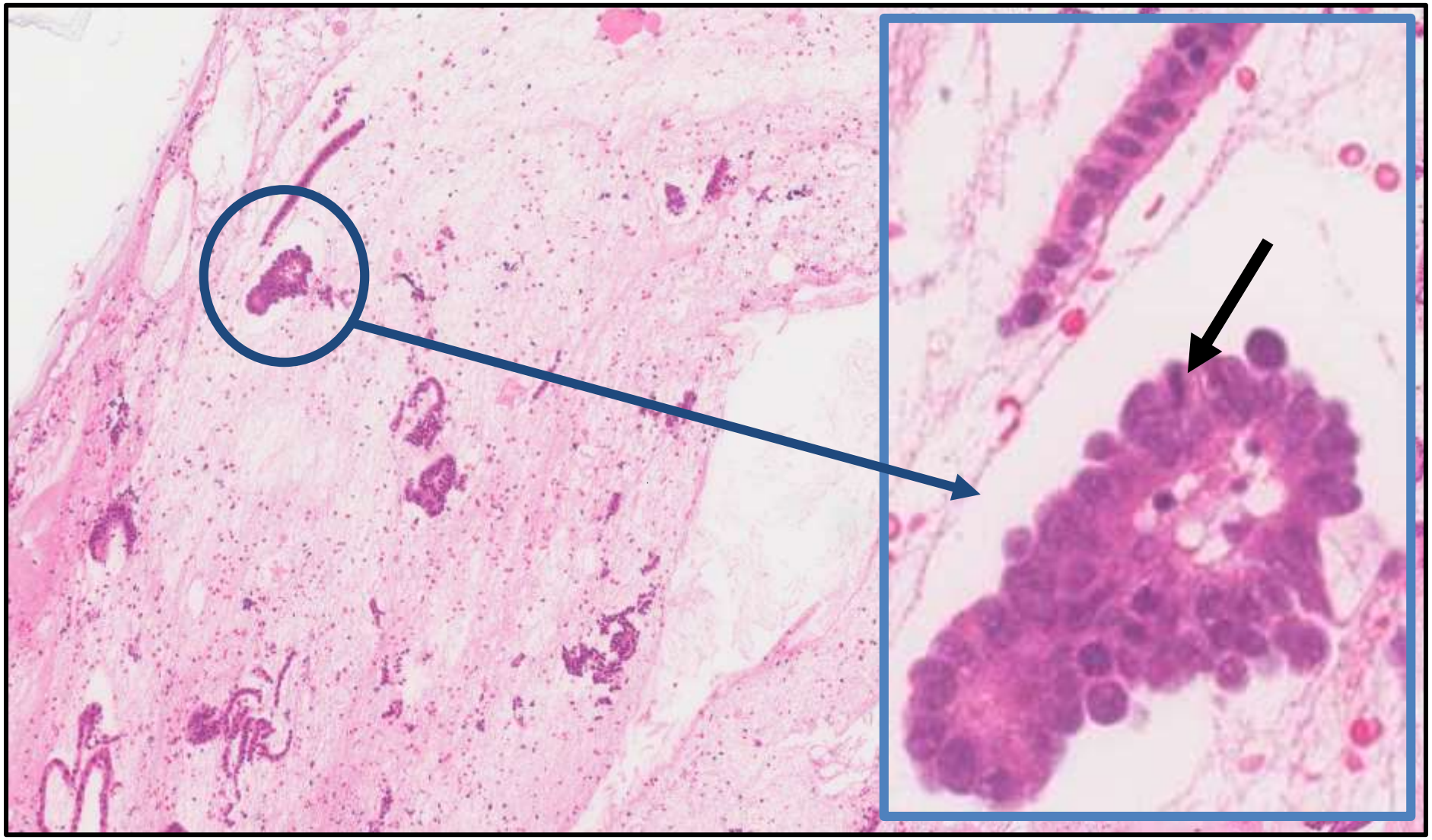
Endometrial biopsy



Endometrial biopsy



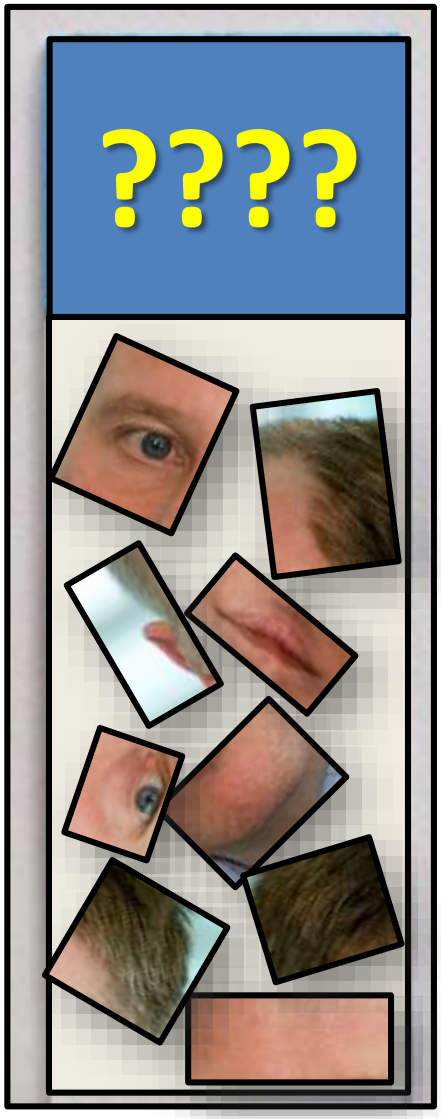
“Snake in the grass”

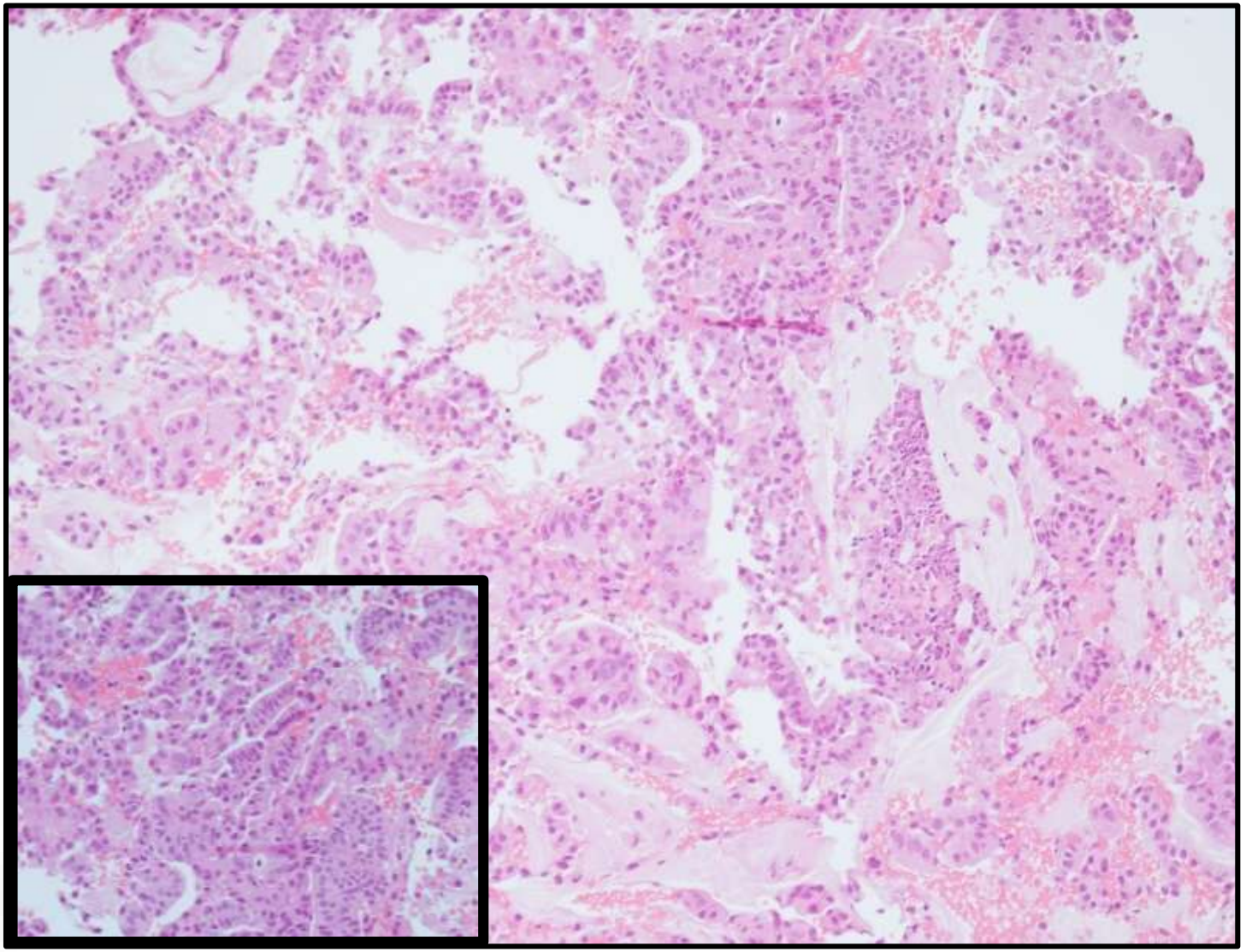


Interpretation issue

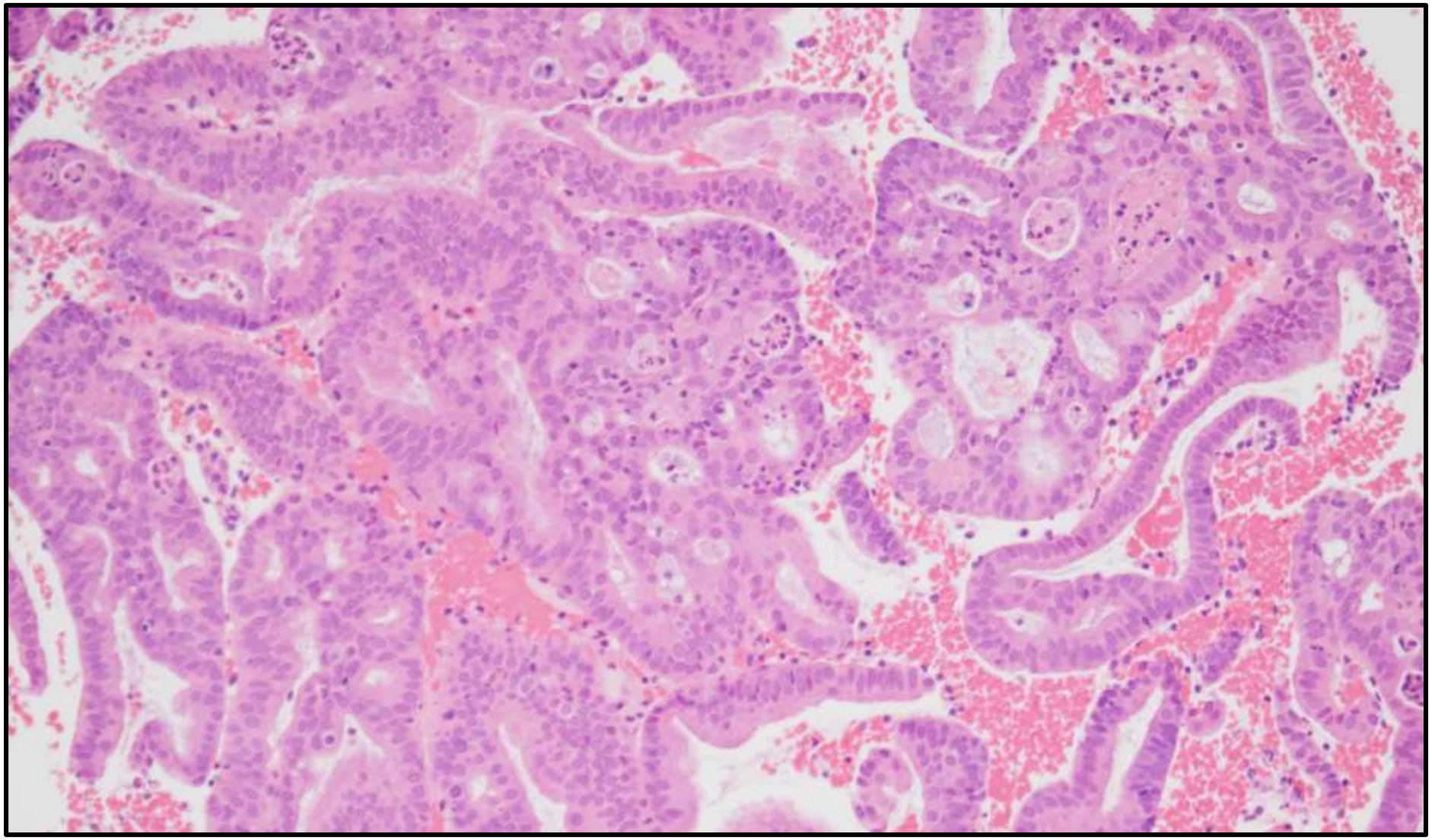
- Very familiar obvious diagnosis difficult on limited material
- Less familiar diagnosis may be difficult even with more generous material
- Diagnosis is more difficult in fragmented specimens

Fragmented material





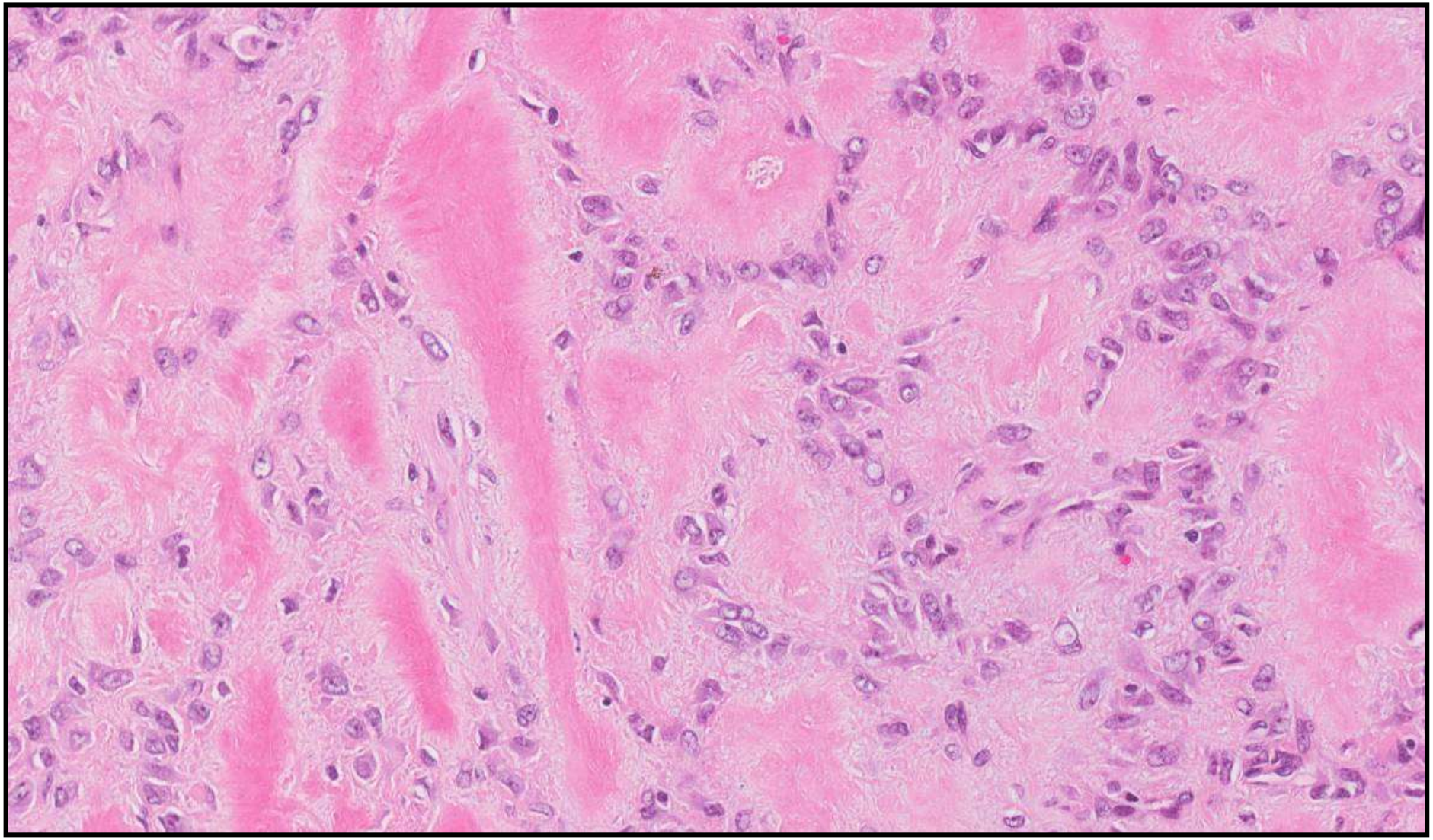
Re-bx: Endometrioid adenocarcinoma



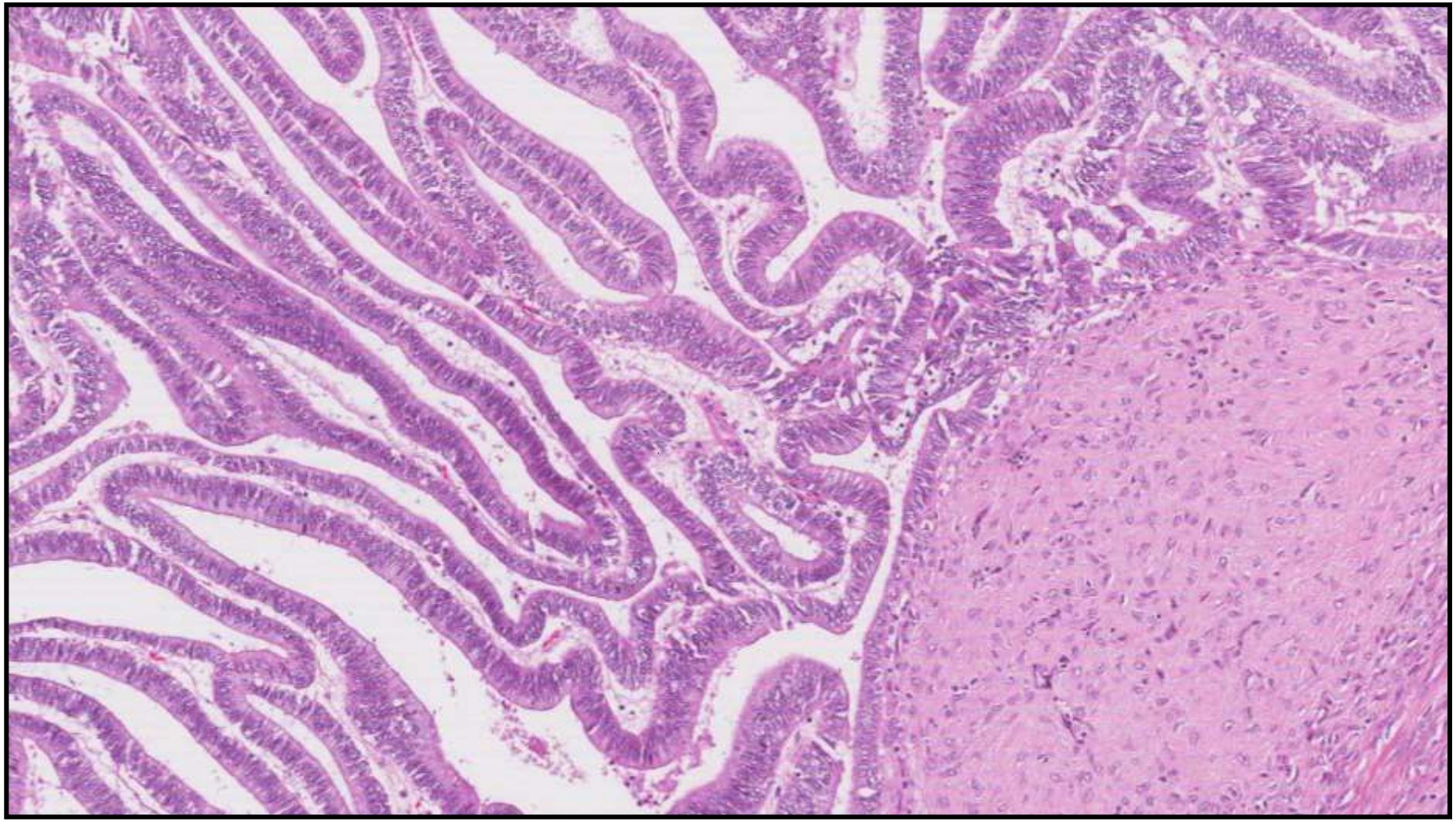
Interpretation issue

- Very familiar obvious diagnosis difficult on limited material
- Less familiar diagnosis may be difficult even with more generous material
- Diagnosis is more difficult in fragmented specimens
- Experts may be able to suspect diagnosis on limited material from rare tumours

Endometrial bx: PMB

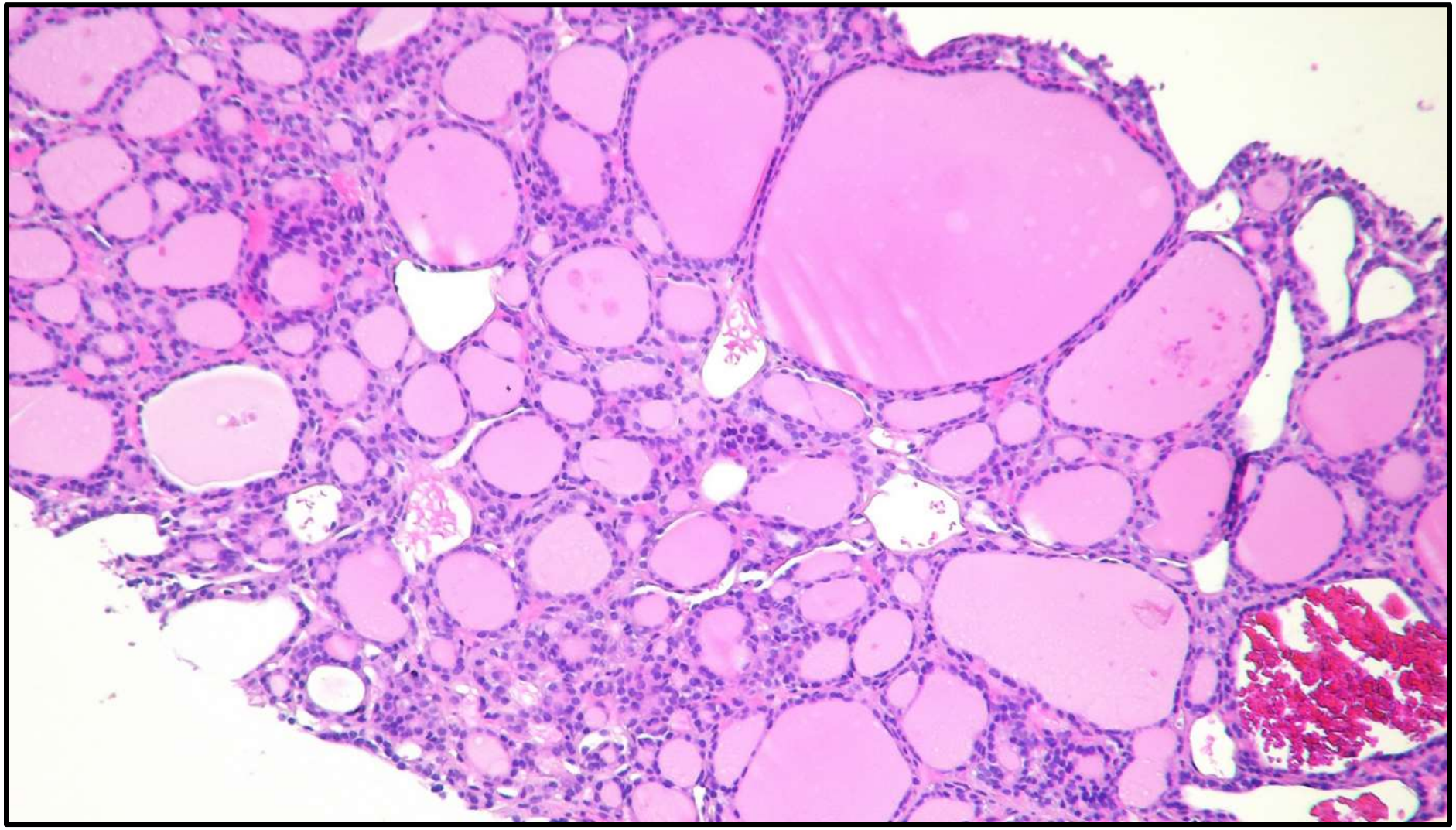


Corded and hyalinised variant of endometrioid ca (CHEC)



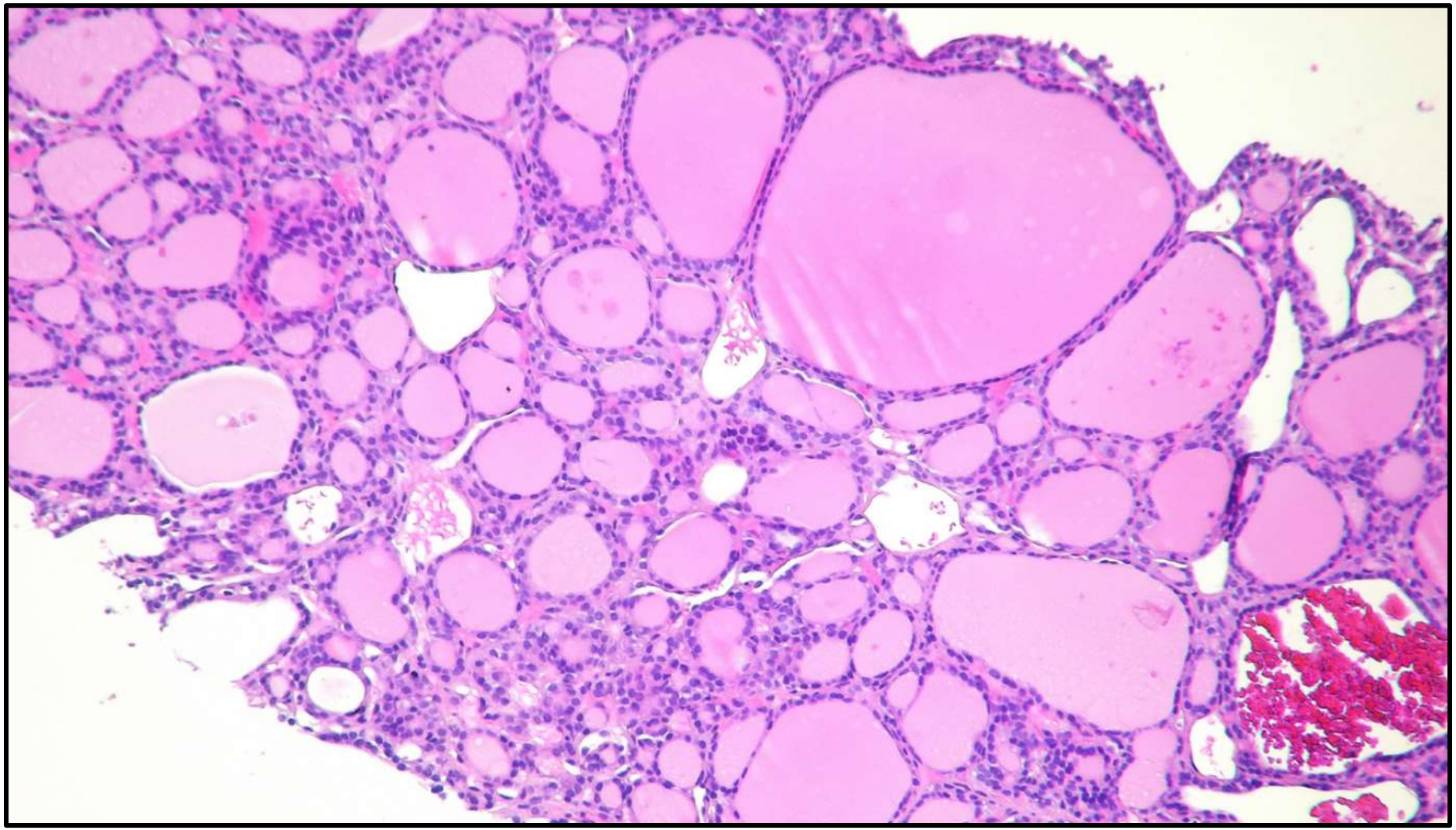
Interpretation issue

- Very familiar obvious diagnosis difficult on limited material
- Less familiar diagnosis may be difficult even with more generous material
- Diagnosis is more difficult in fragmented specimens
- Experts may be able to suspect diagnosis on limited material from rare tumours
- Even experts cannot make diagnosis on identical mimics



Vertebral body biopsy

Metastatic follicular carcinoma

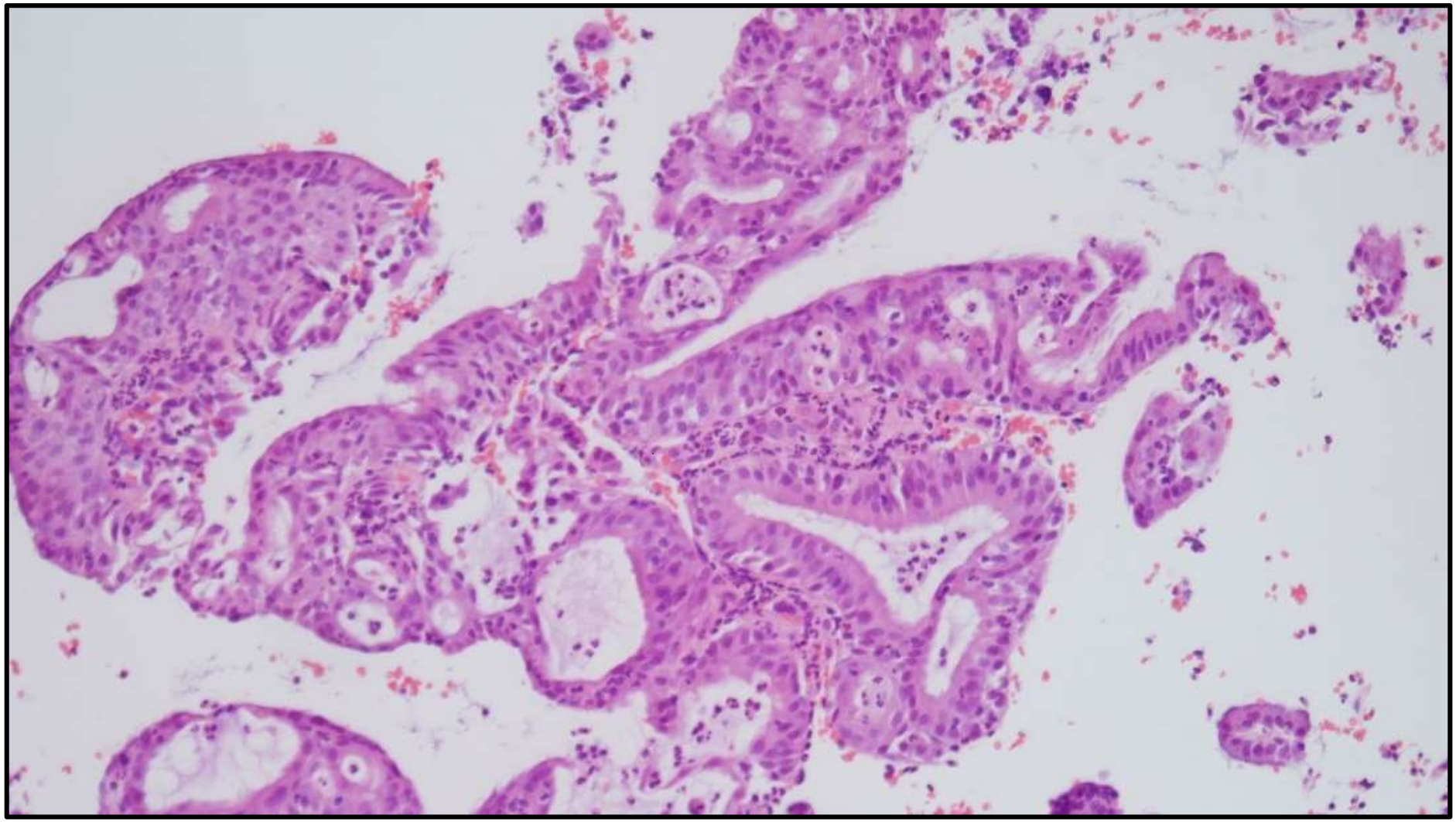


Interpretation issues

- Limited material
- Fragmented material
- **Uncertain topography**
- Background

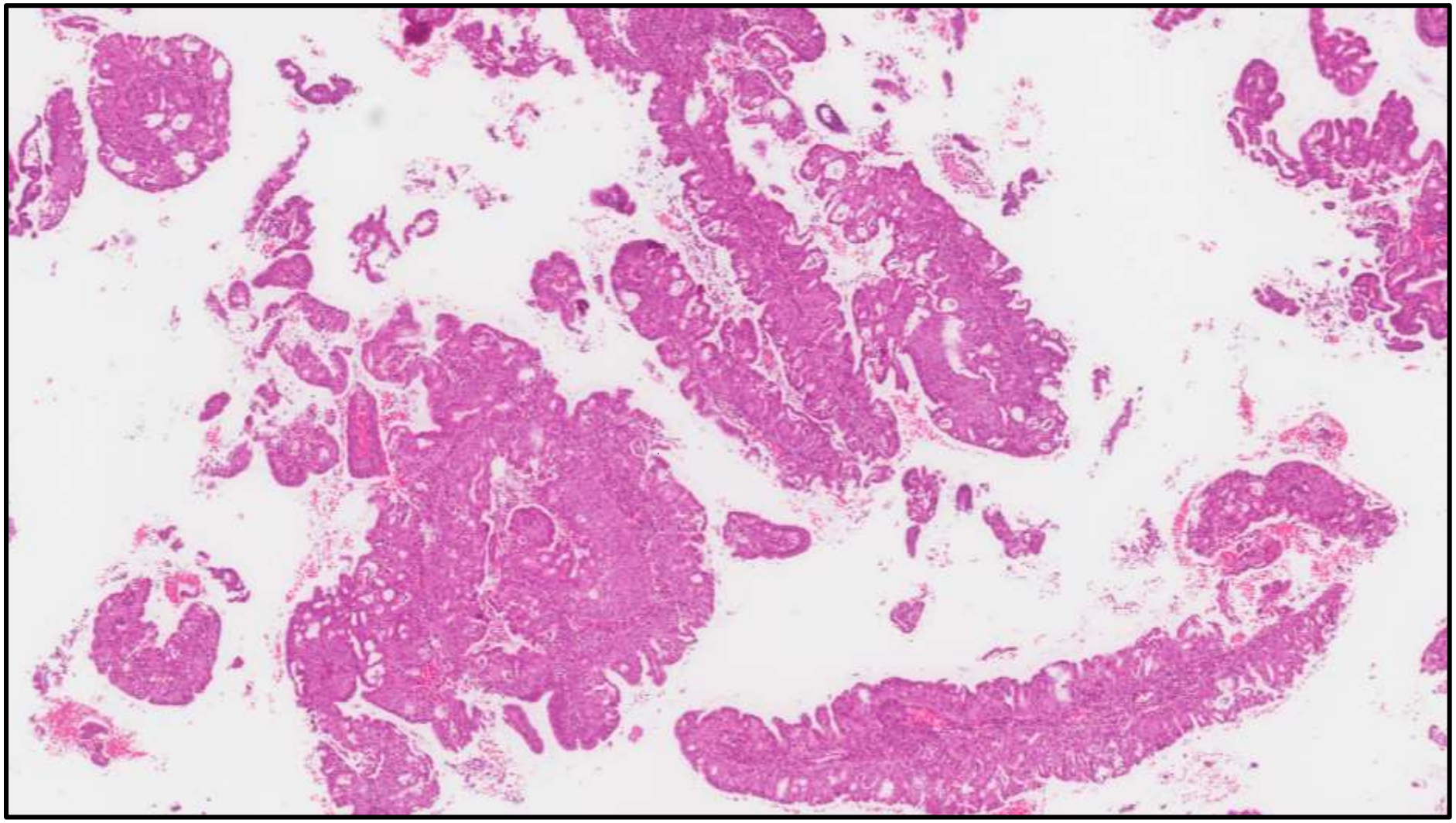
Perimenopausal bleeding

Endometrial bx



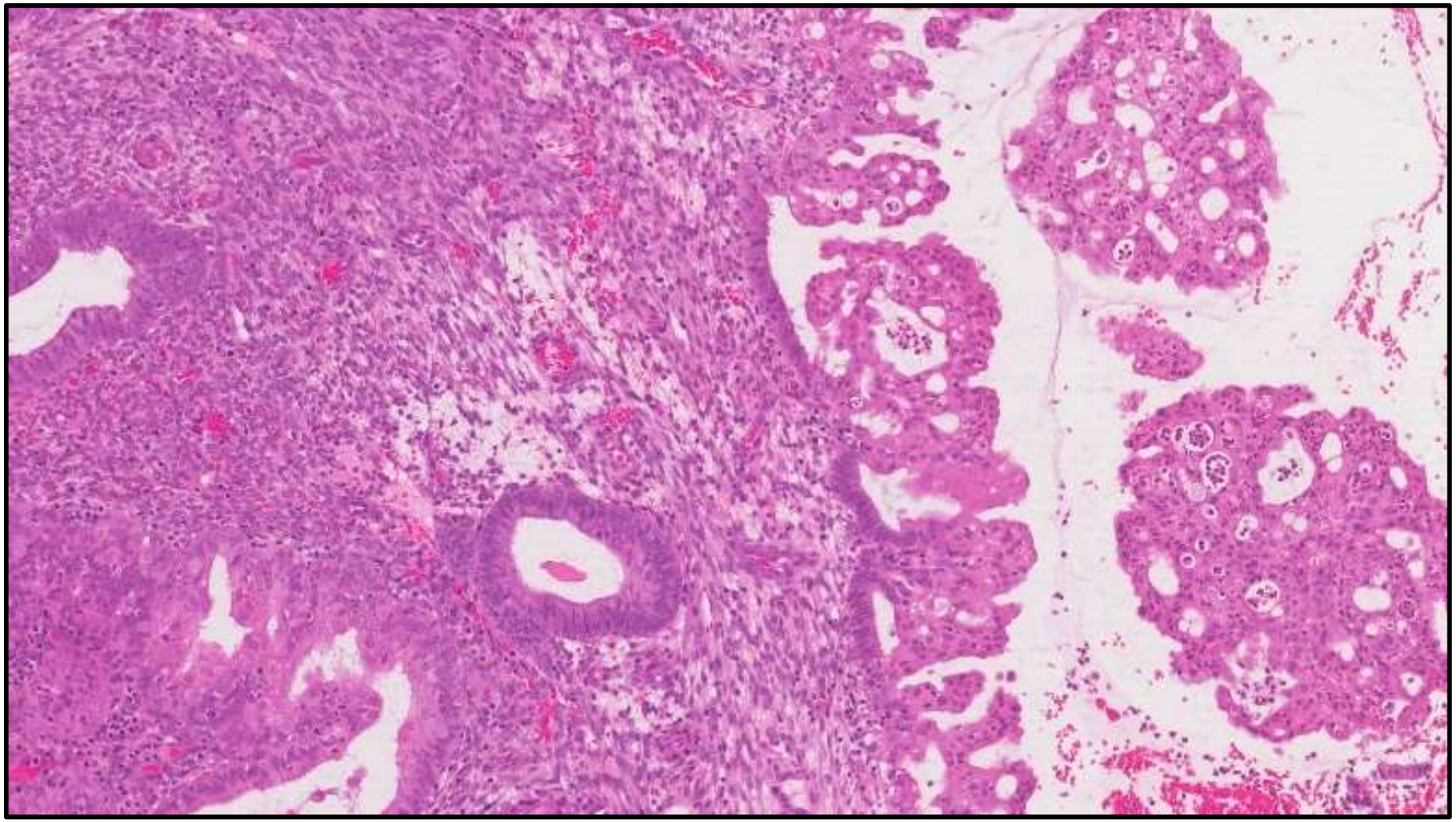
Perimenopausal bleeding

Endometrial bx



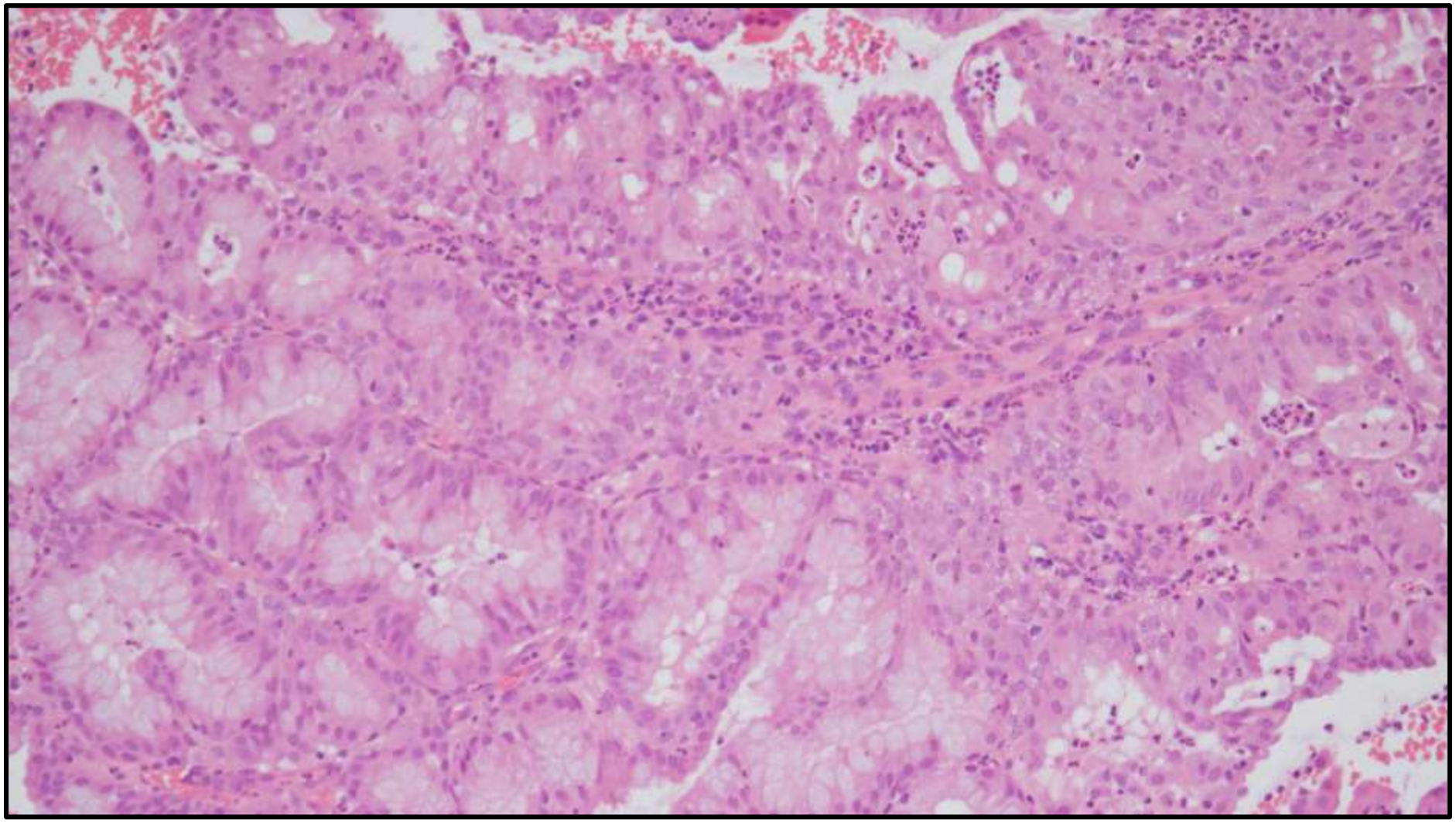
Perimenopausal bleeding

Endometrial bx

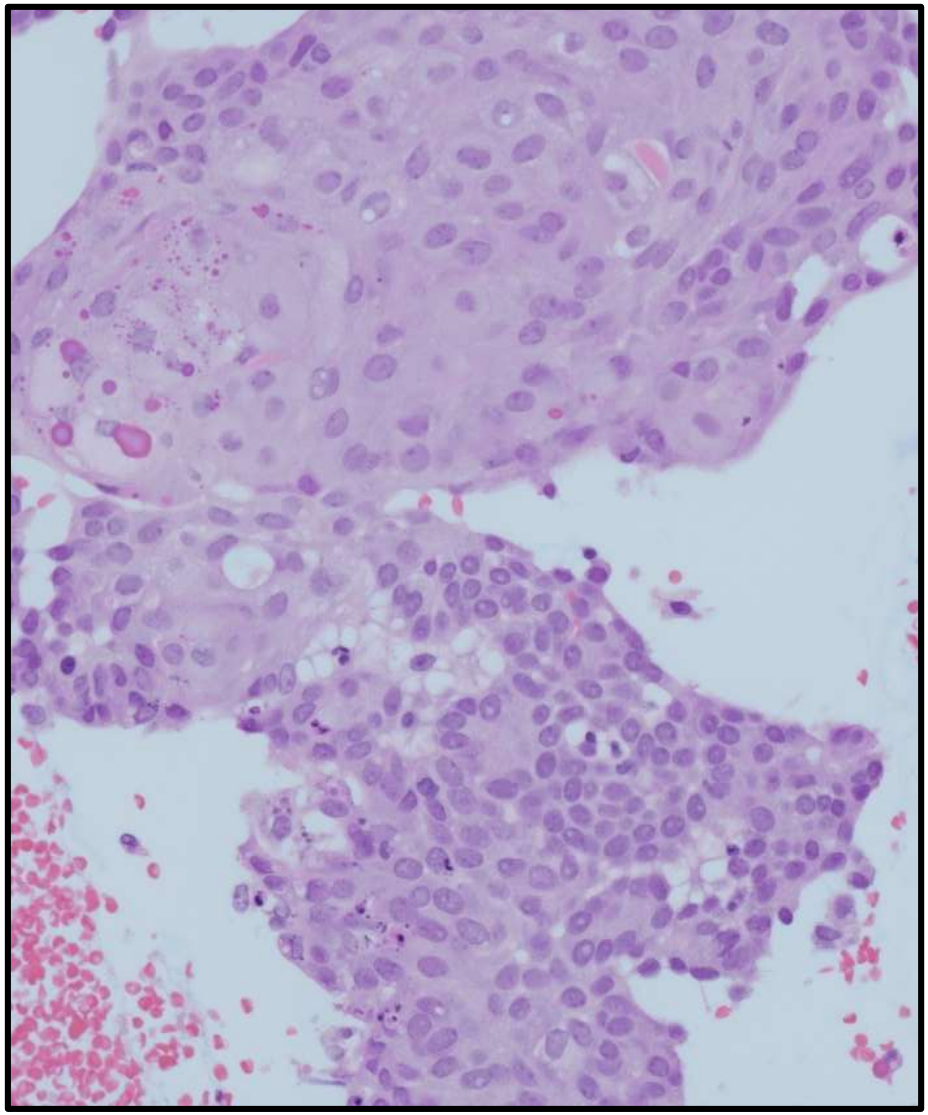


Perimenopausal bleeding

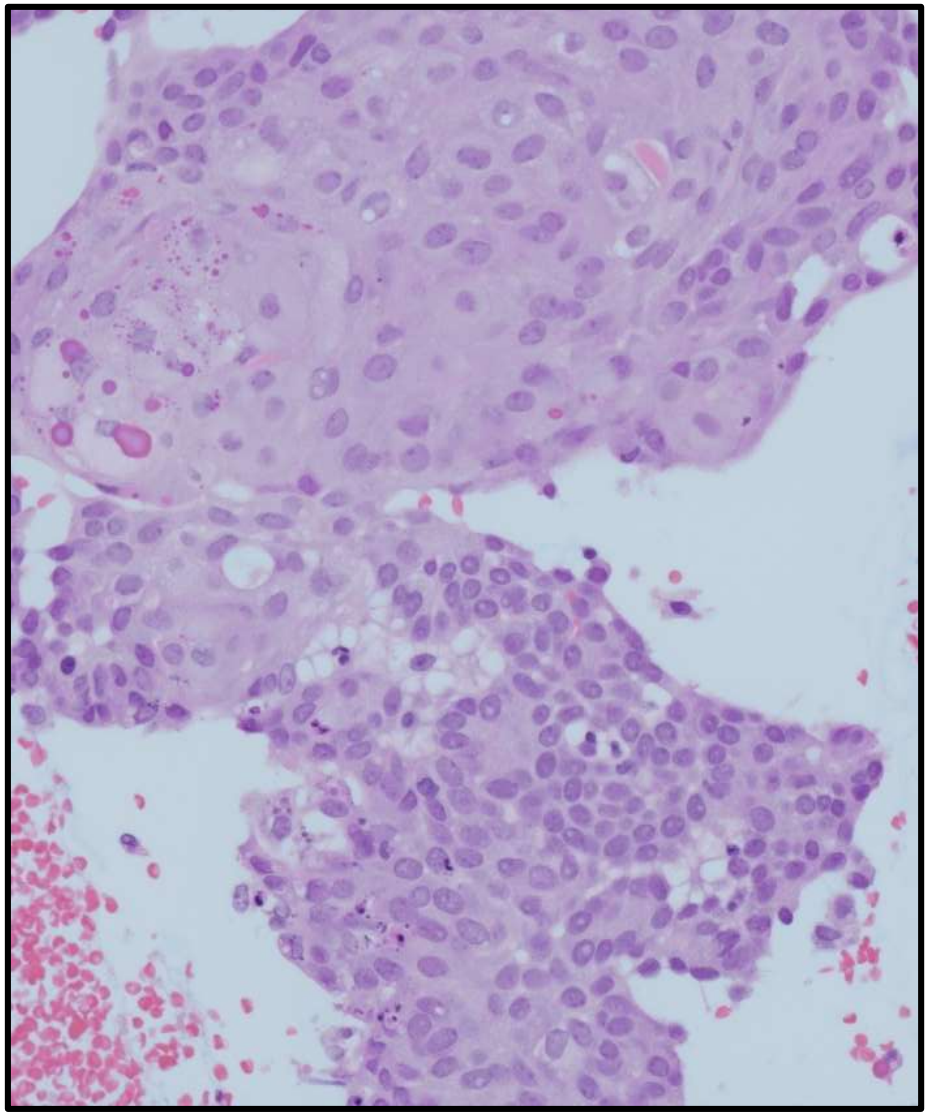
Endometrial bx

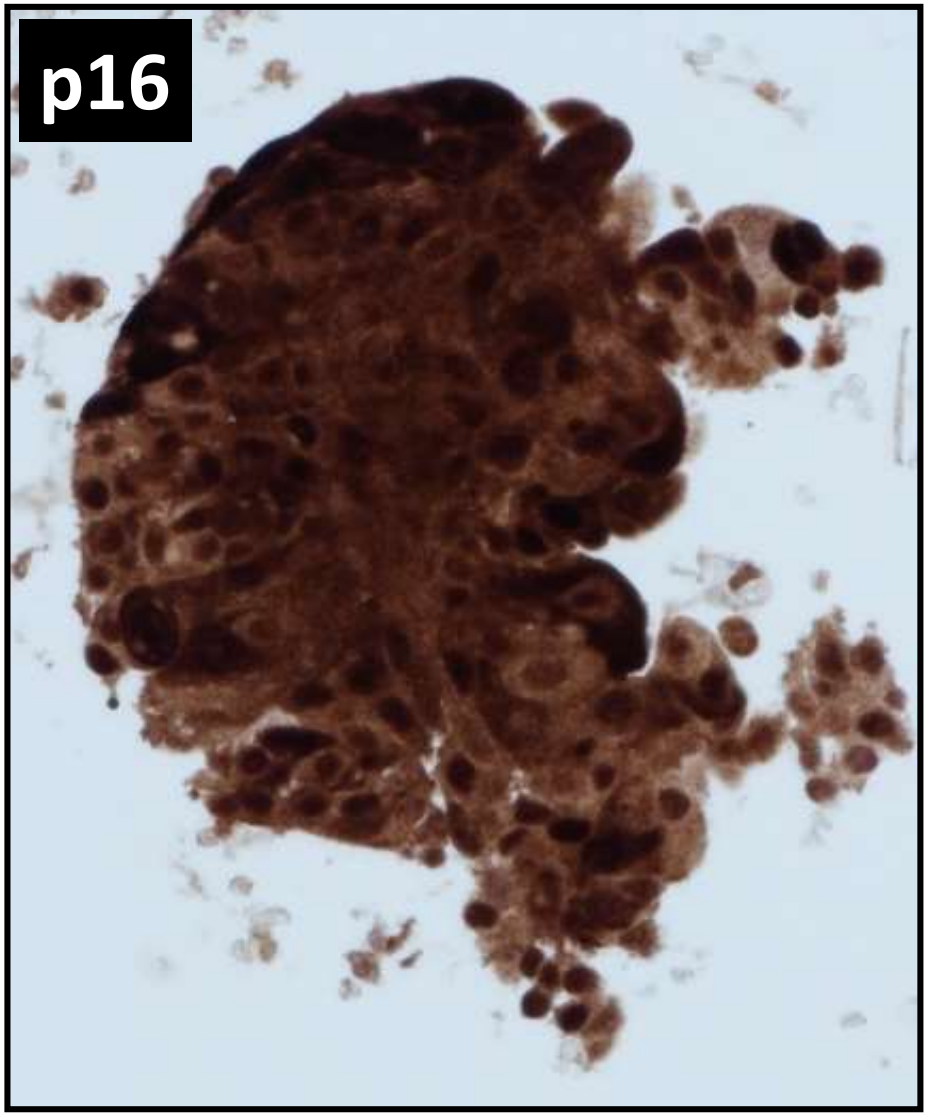


Endometrial biopsy

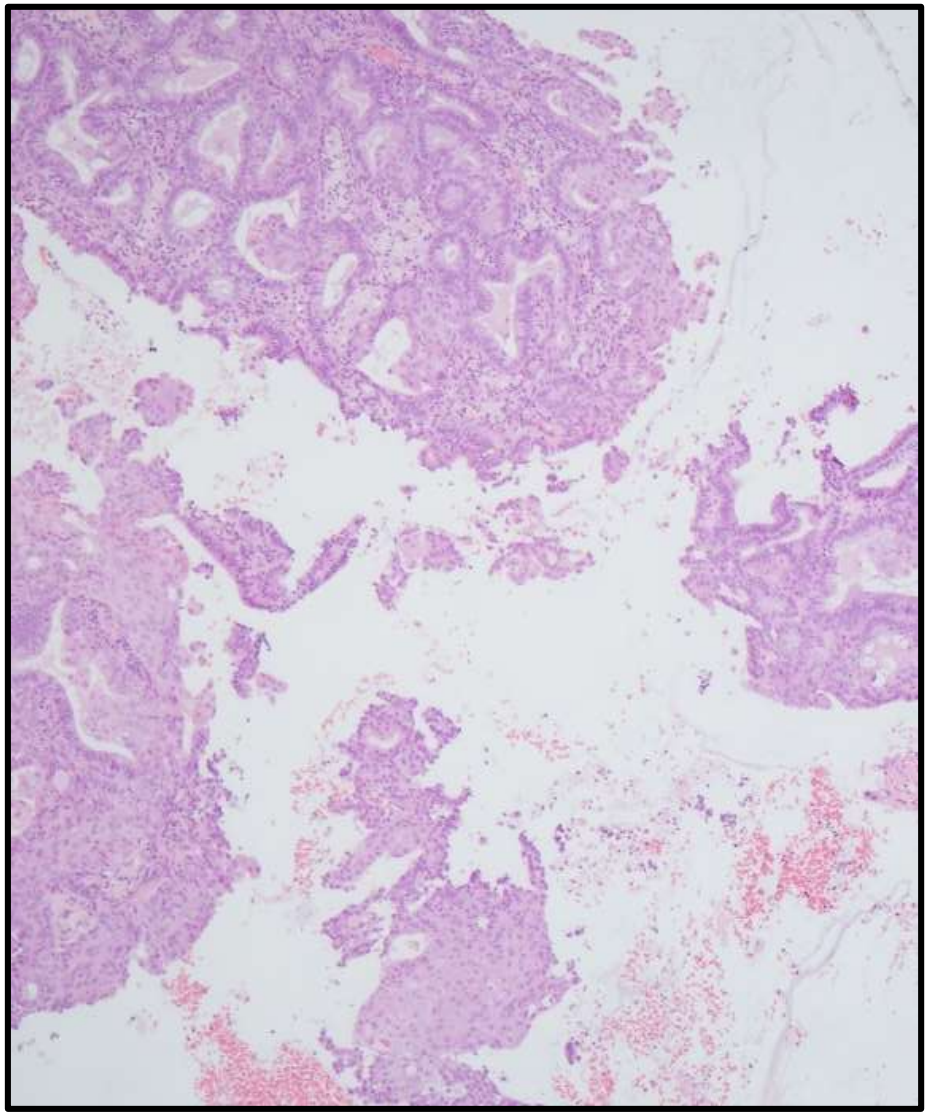


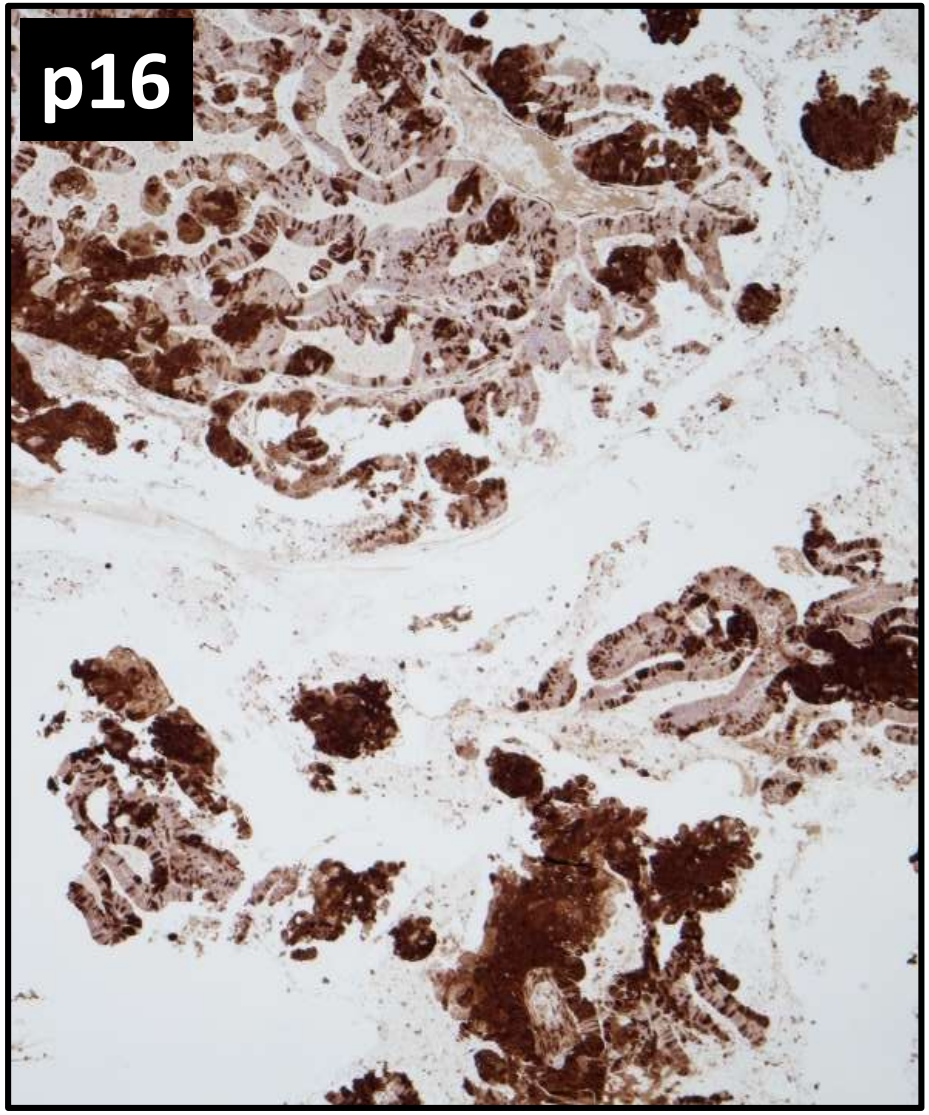
Endometrial biopsy





Endometrioid adenocarcinoma with squamous morules





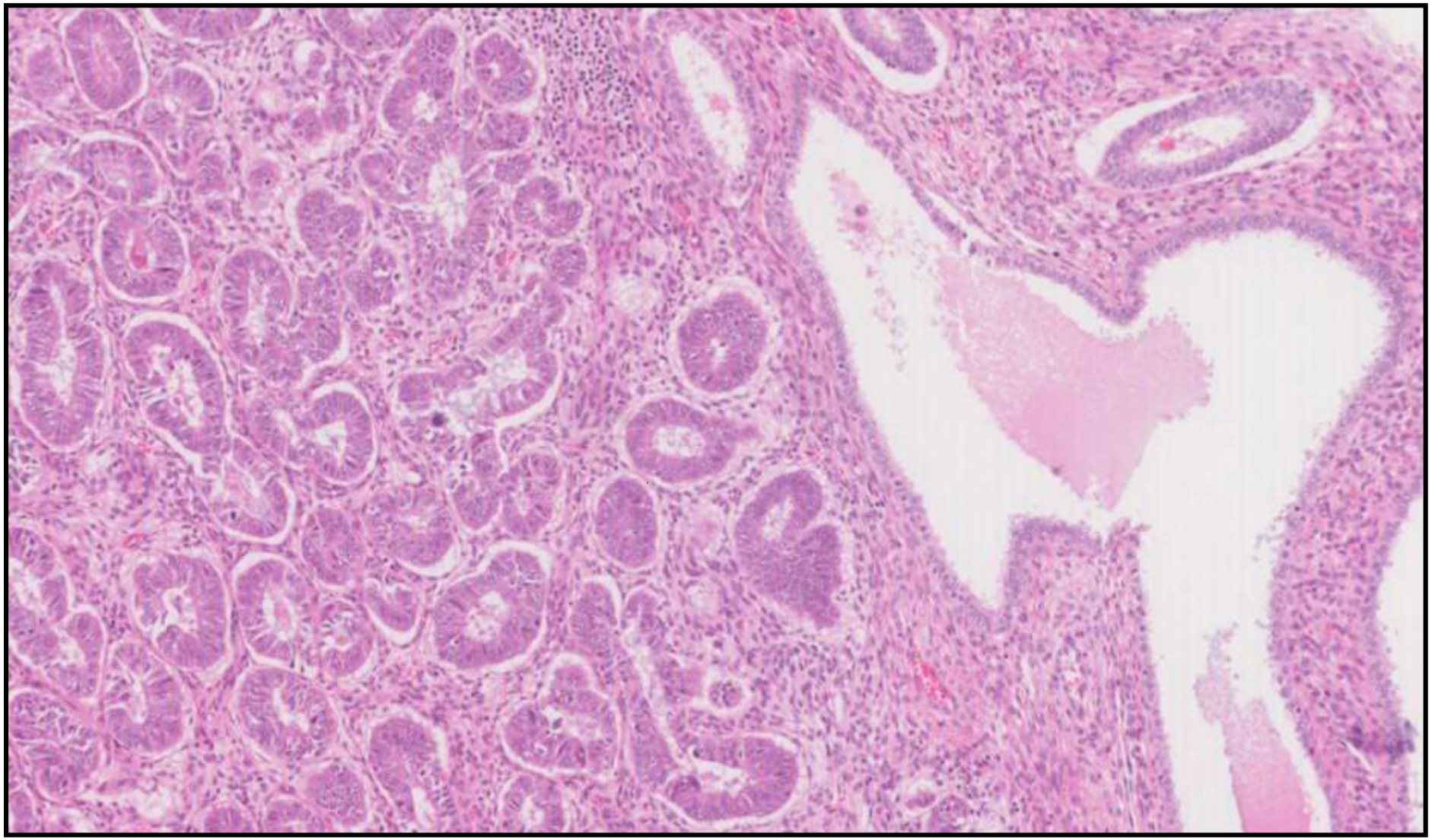
Identification more difficult

- Limited material from a familiar tumour
  - Especially less diagnostic area
- Unfamiliar tumour even with more generous material
- Morphological mimic
- Uncertain location

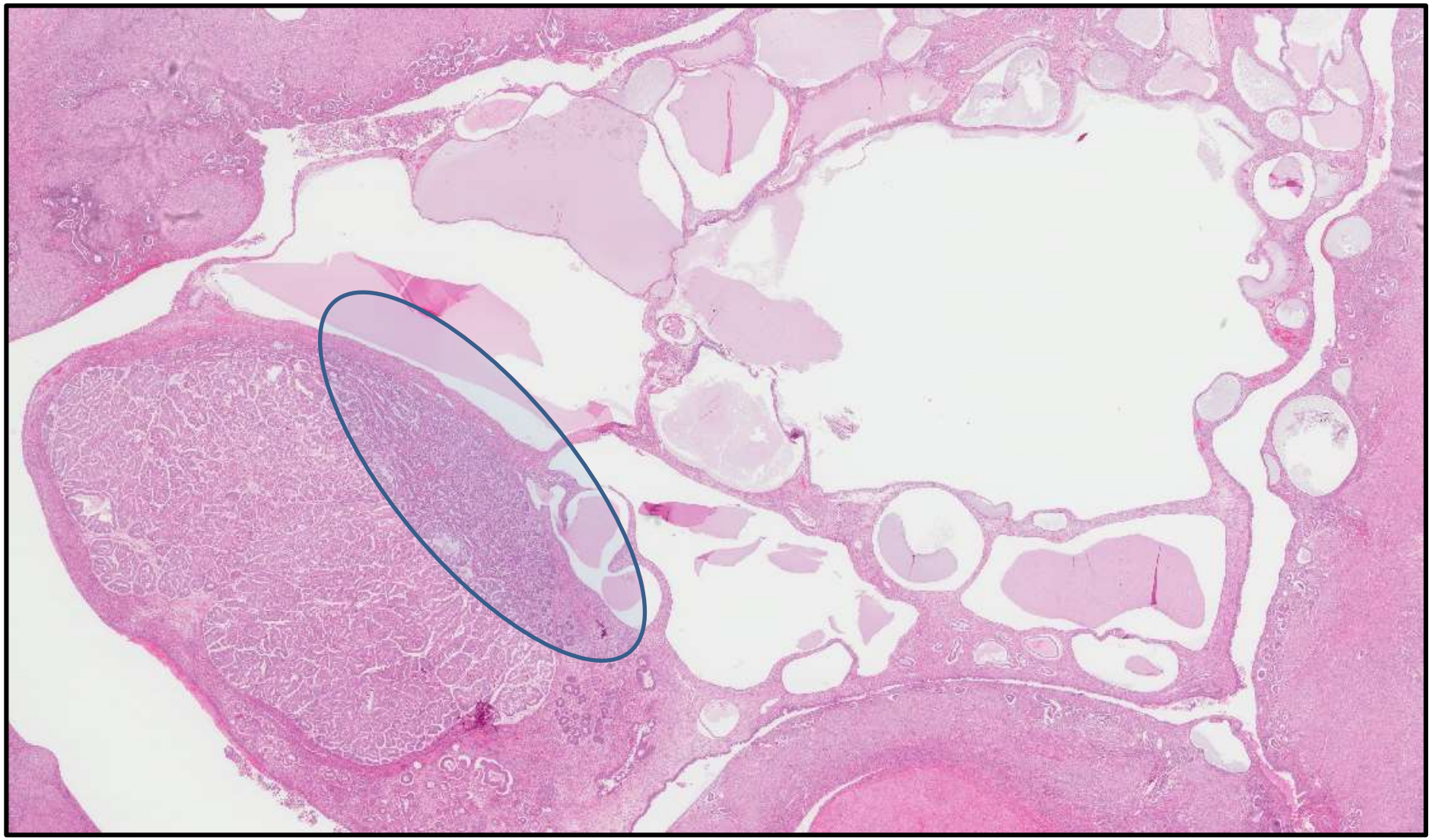
Small biopsies

Interpretation issues

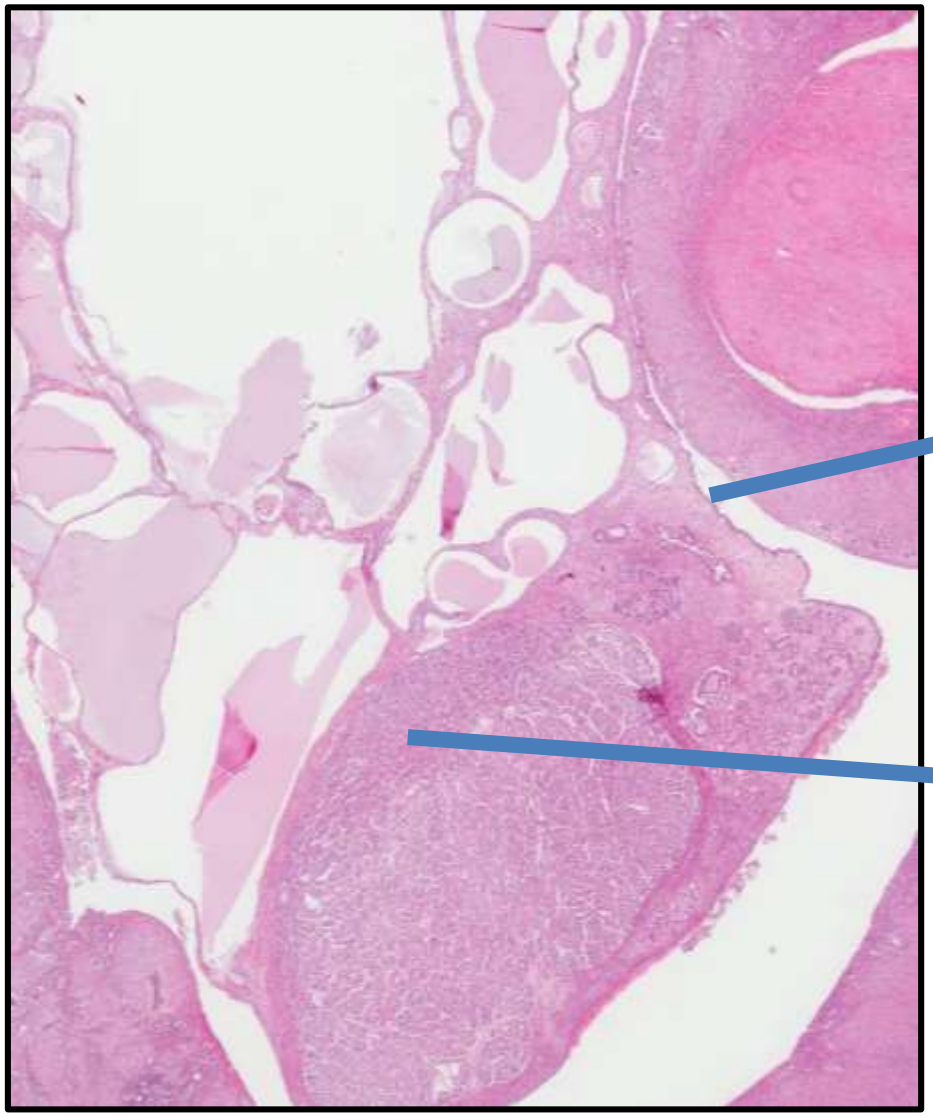
- Limited material
- Fragmented material
- Uncertain topography
- **Background**

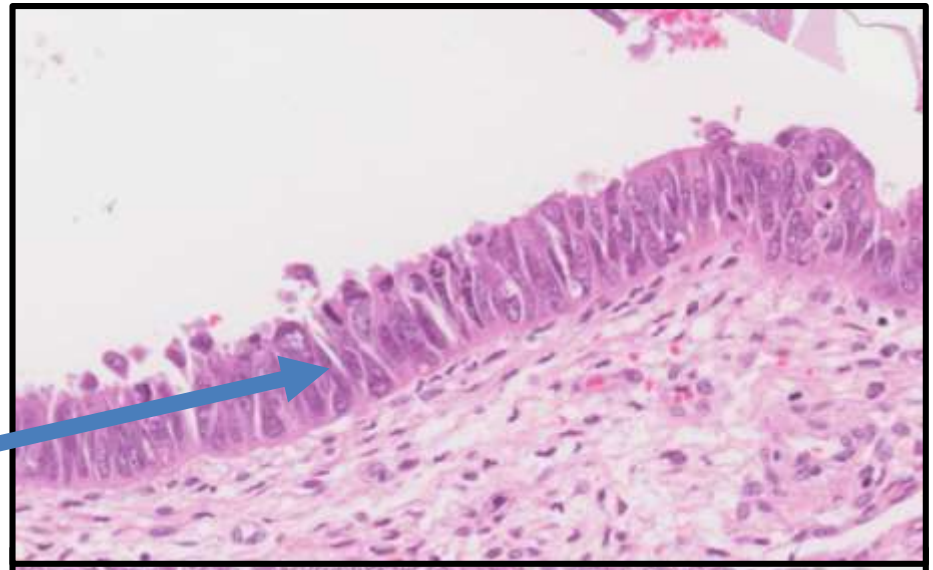


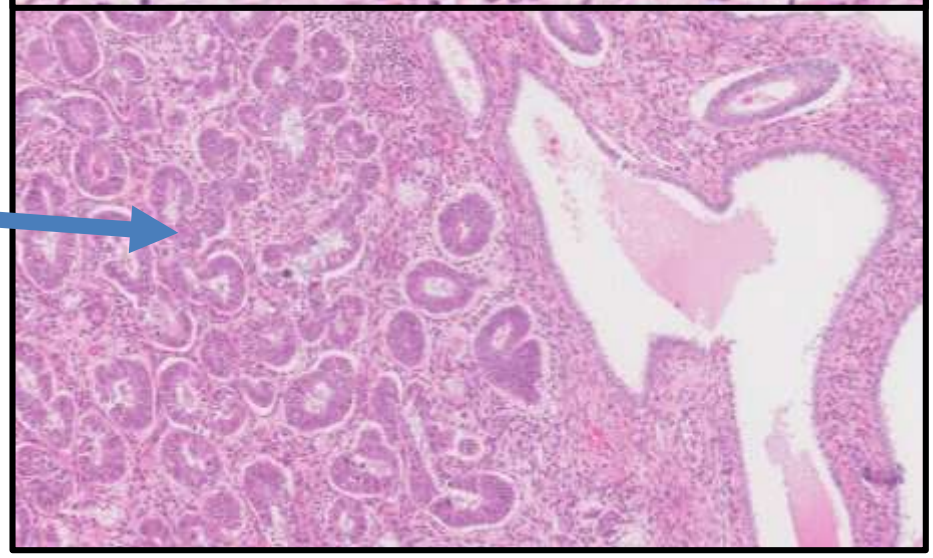
Atrophic endometrial polyp



“Right background”







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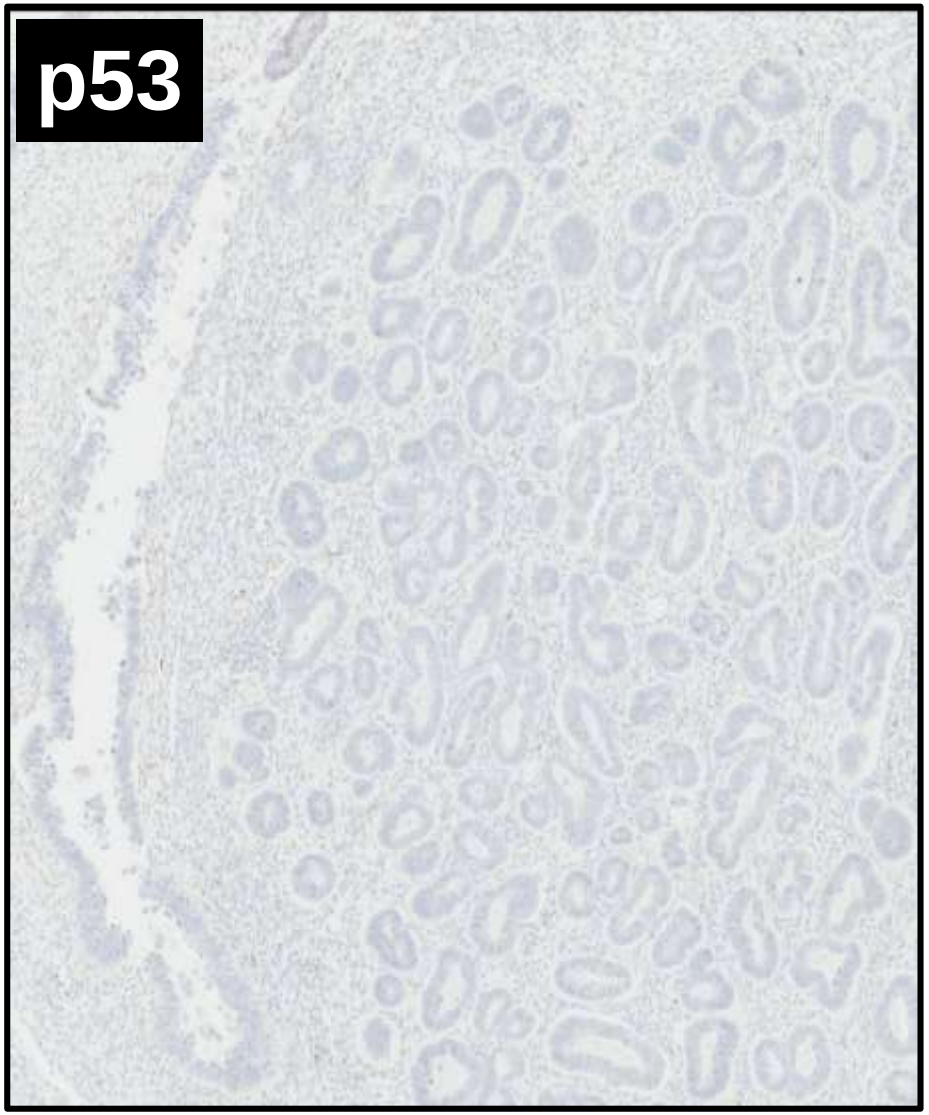

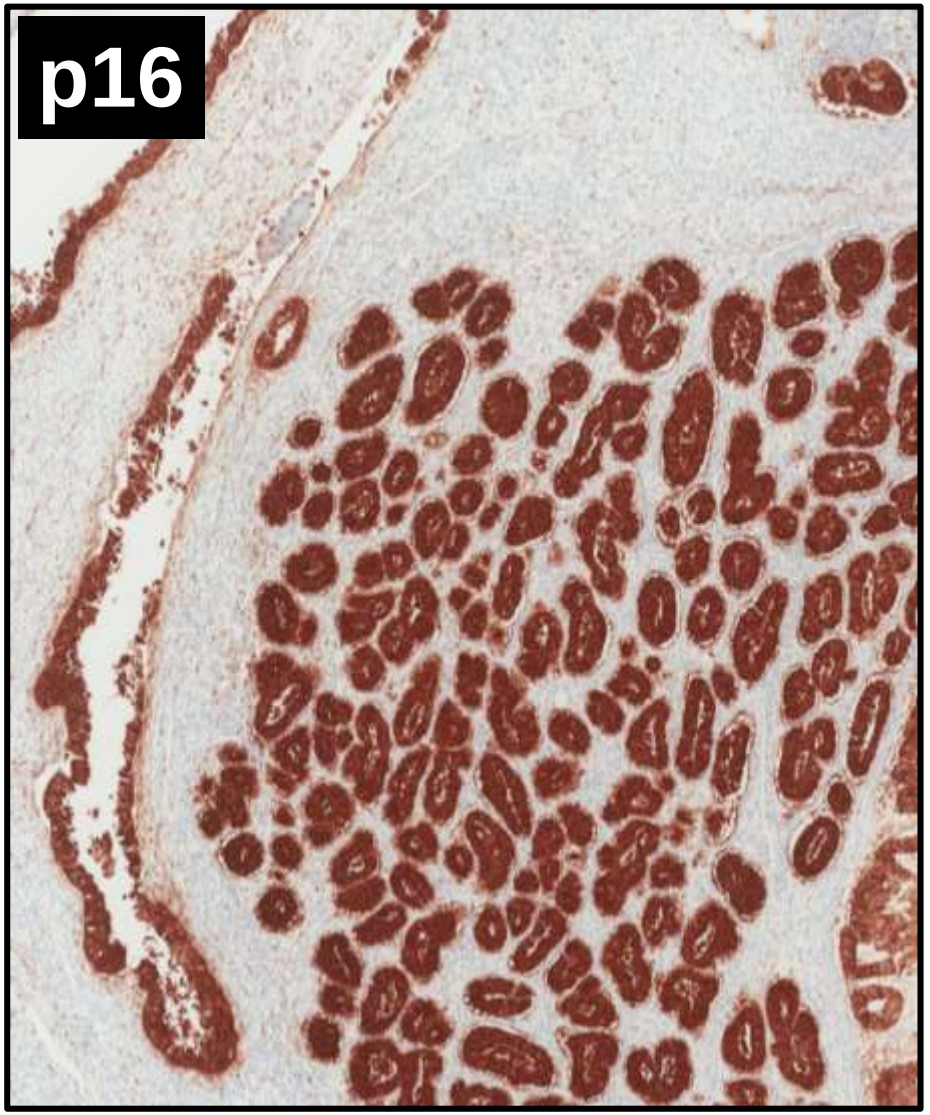

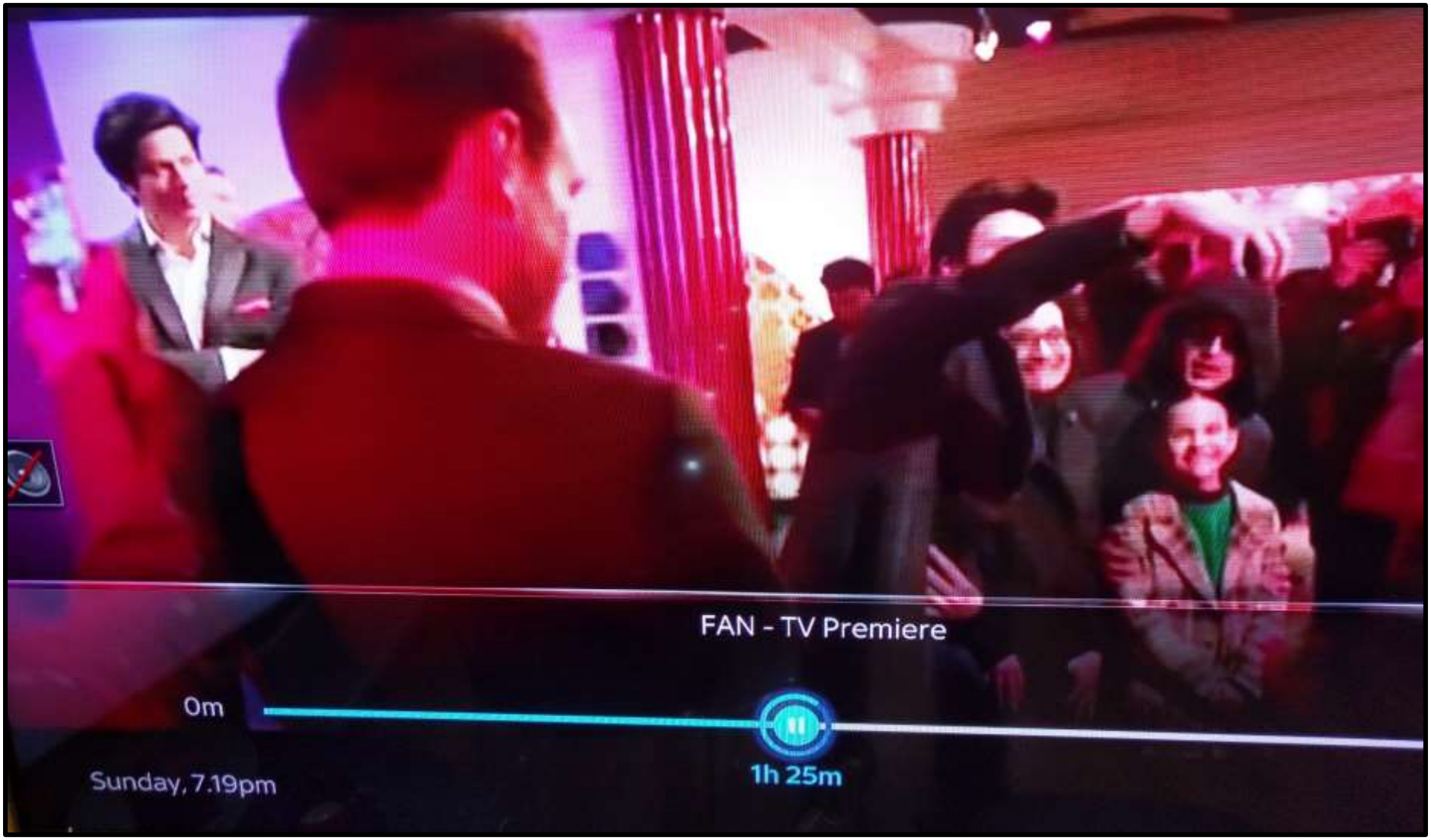
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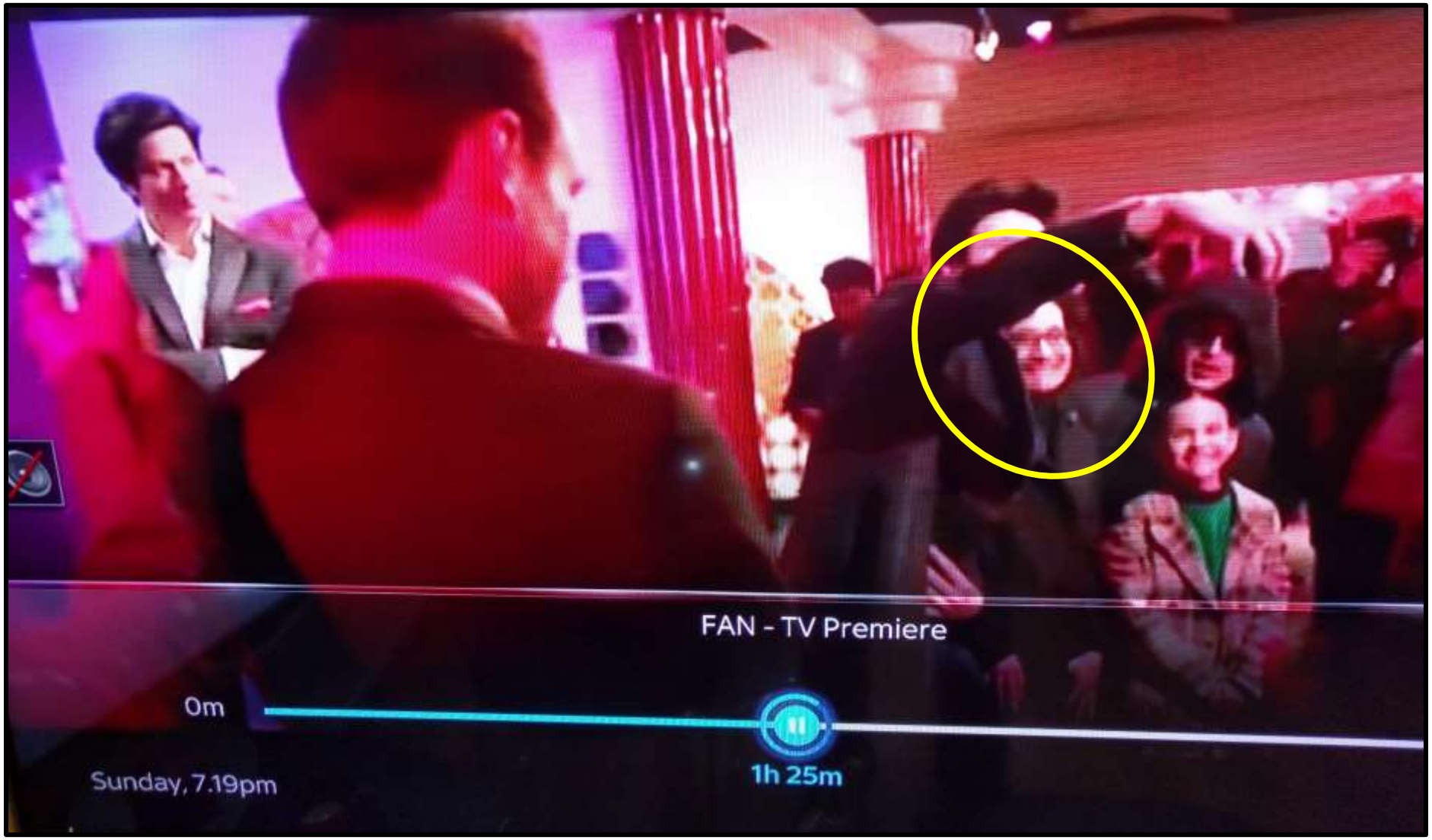
1h 25m
Sunday, 7.19pm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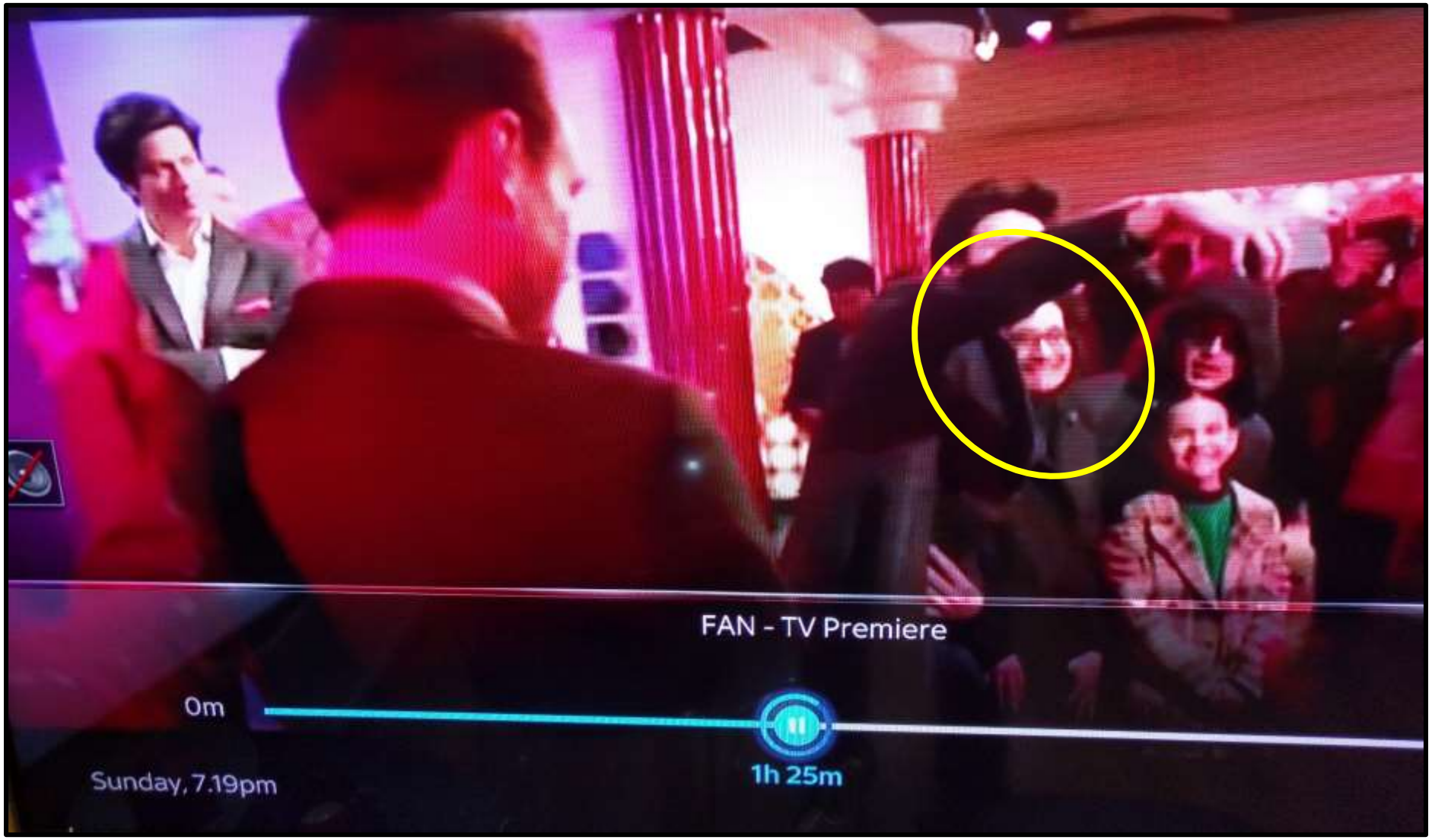
1h 25m
Sunday, 7.19pm

Misleading background



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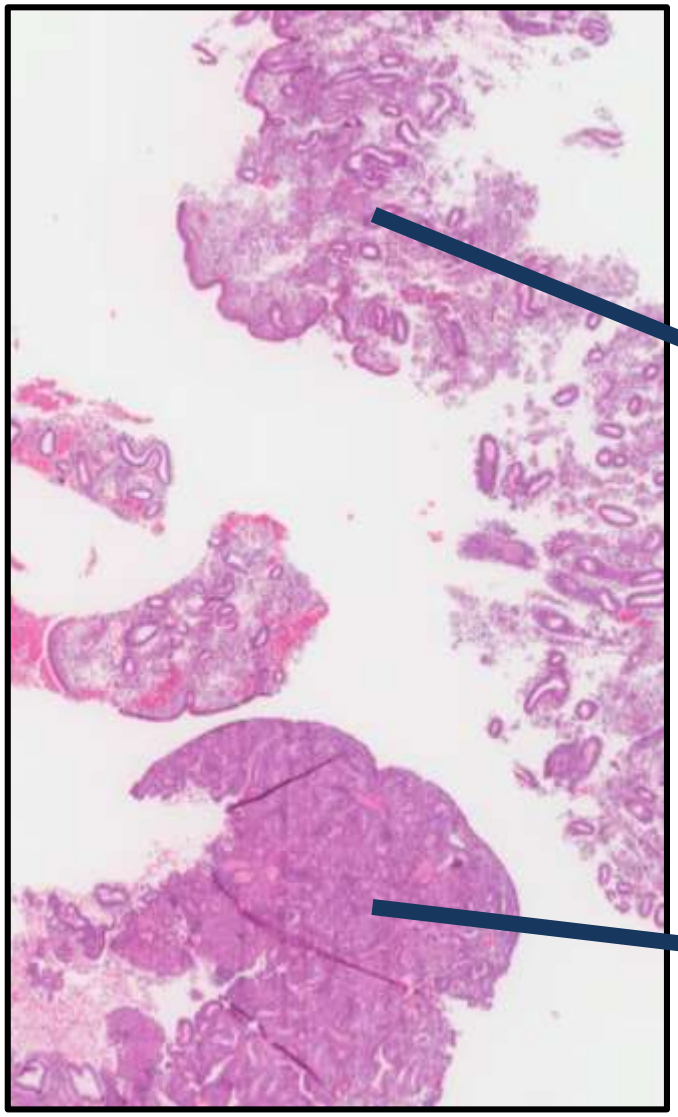
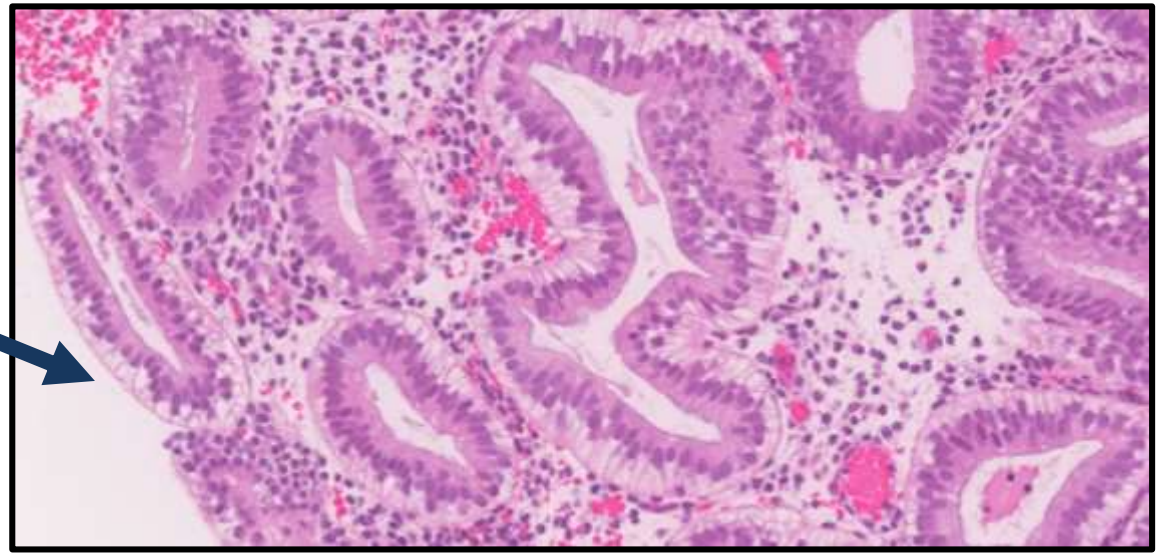
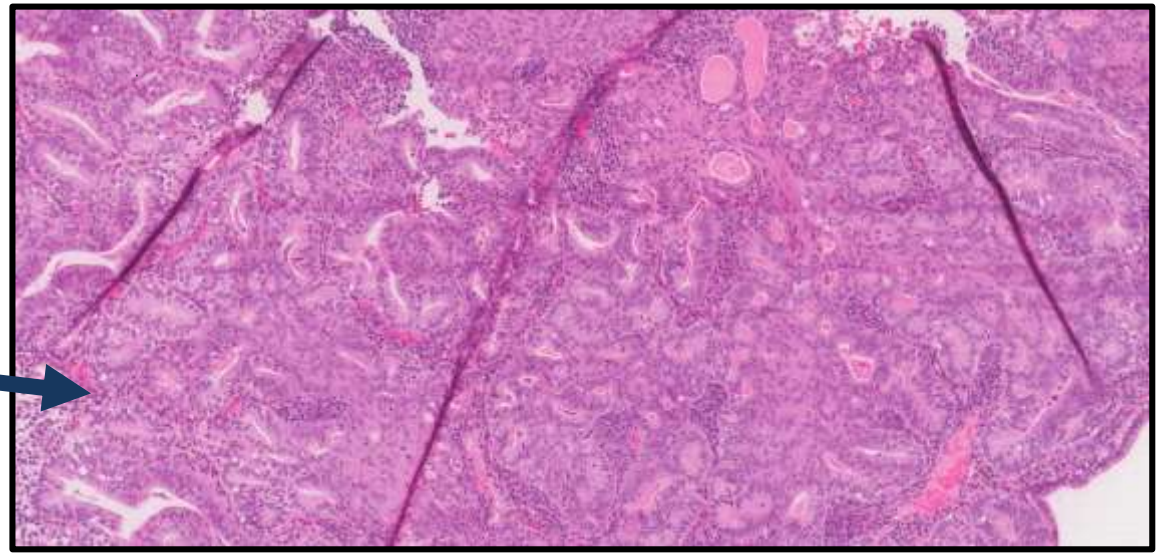




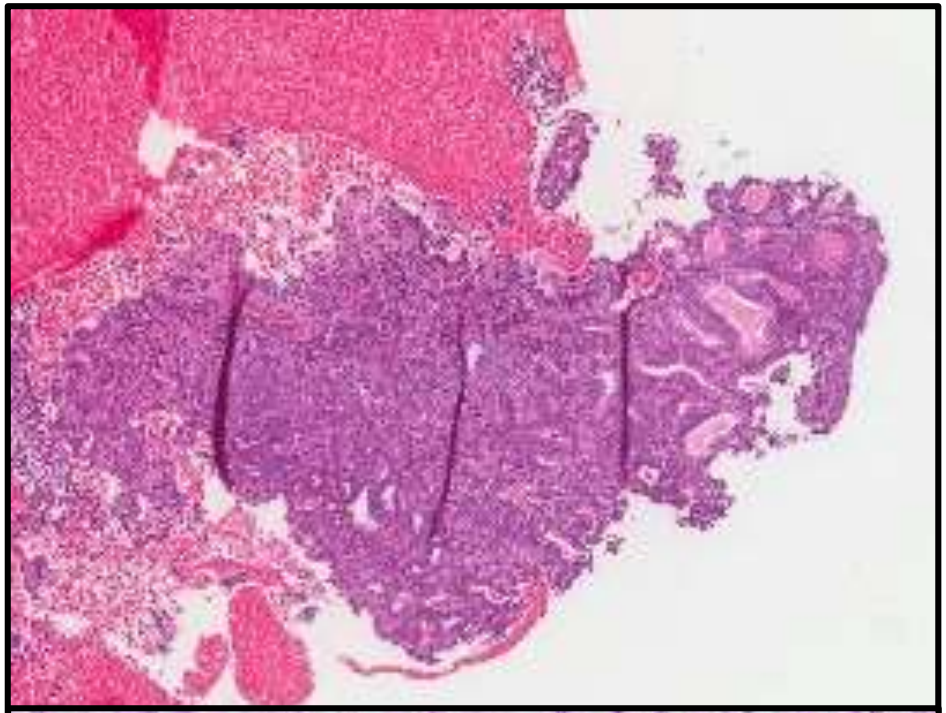


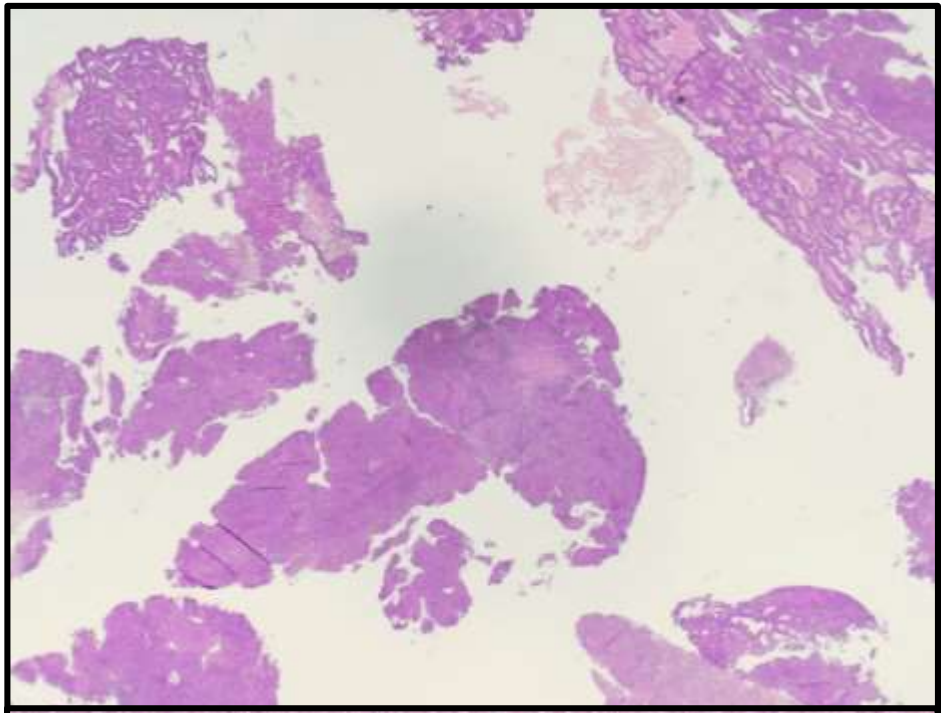
Smaller Tissues: Larger Issues

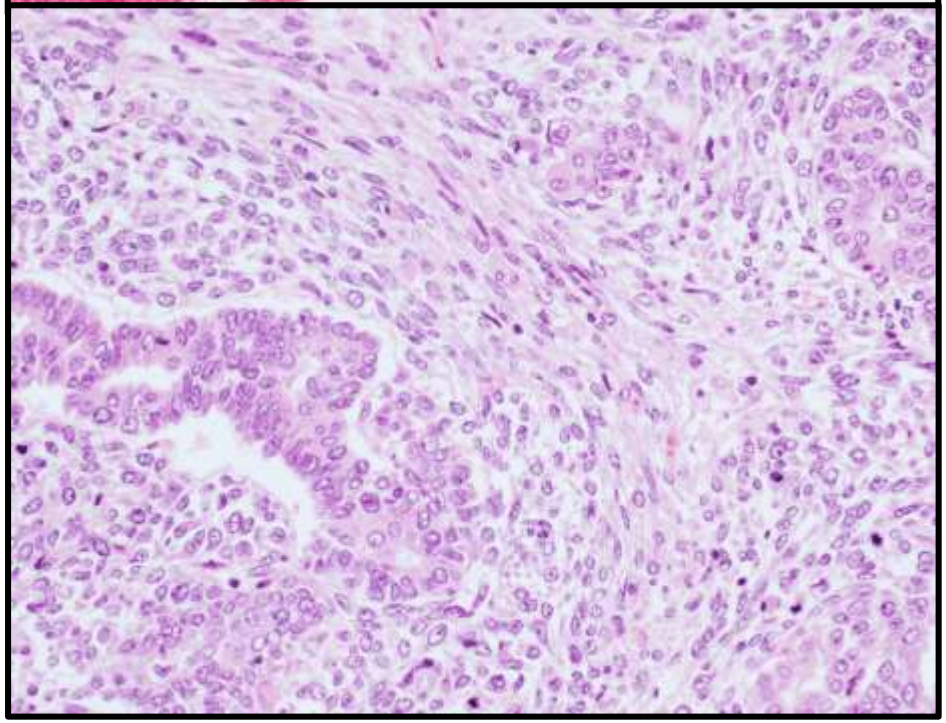
- Interpretation issues
- **Sampling issues**
- Handling issues
- Time constraints
- Clinical implications

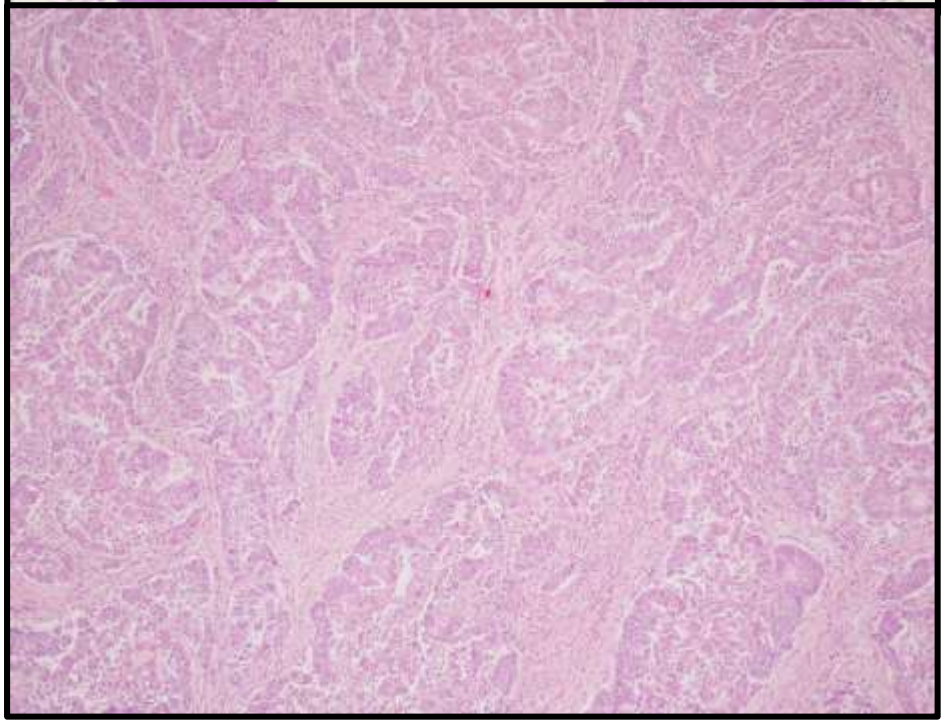
Endometrial bx

- **Luminal component sampled by bx may not be representative**
  - Myoinvasive component may be of different grade

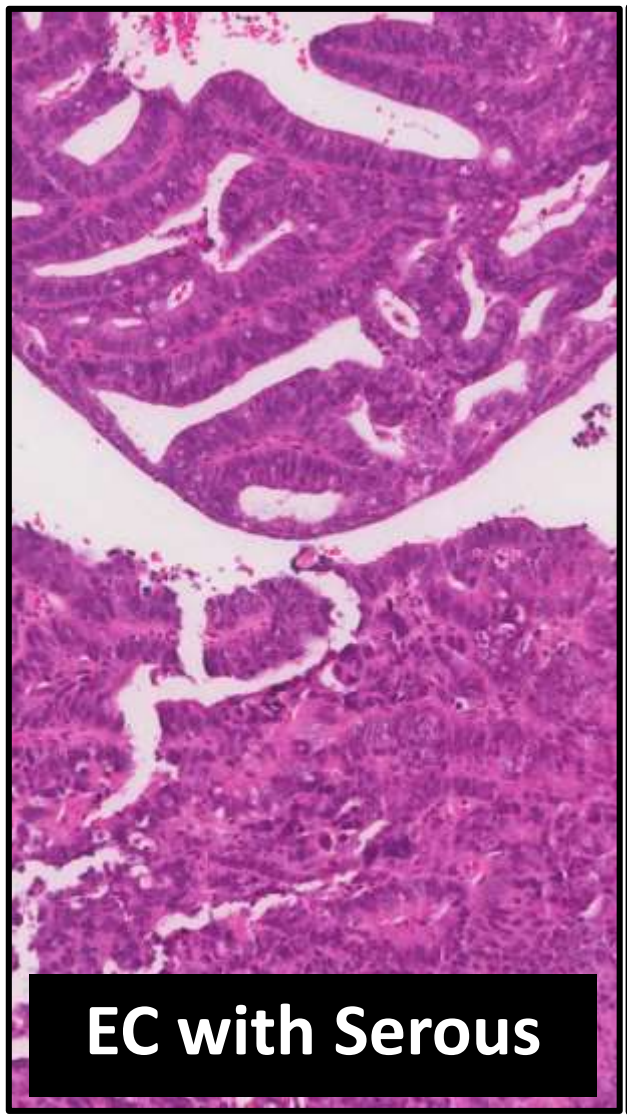


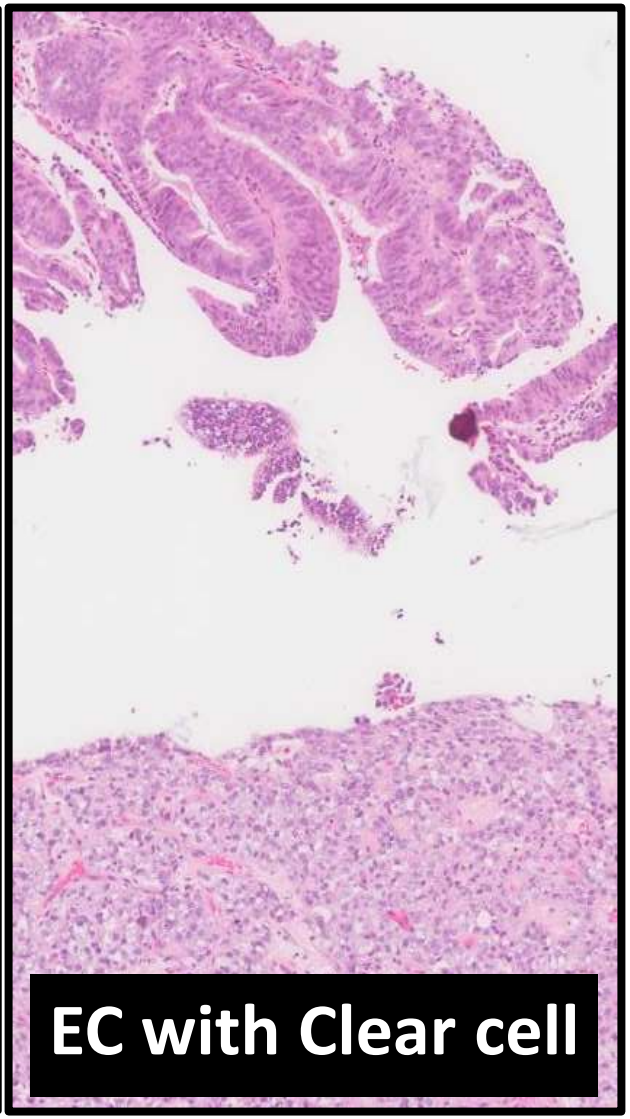


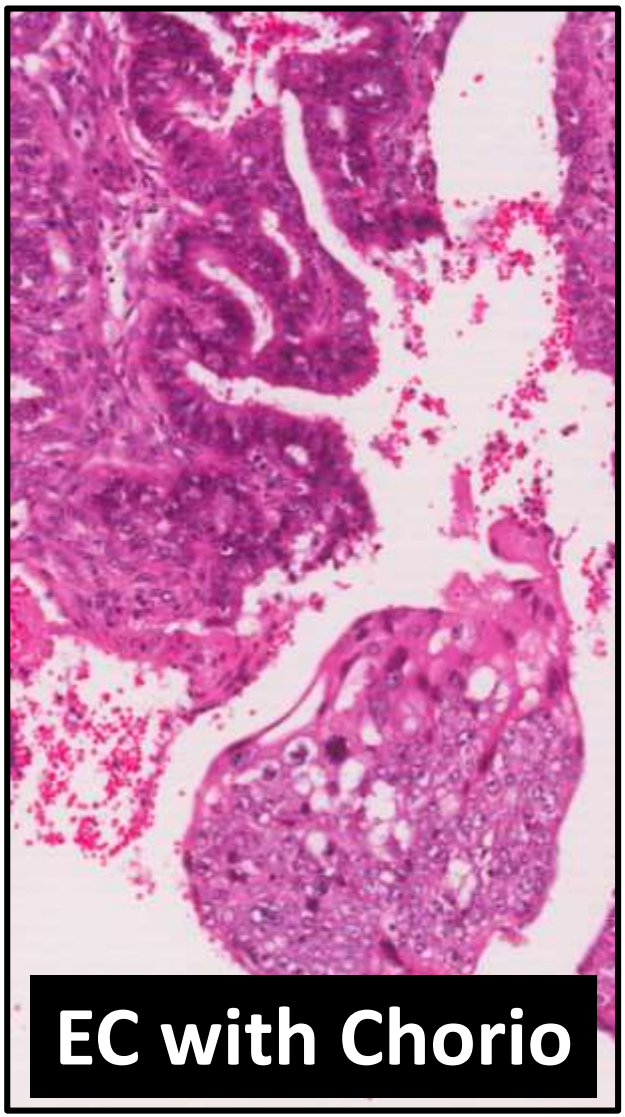




Mixed carcinomas



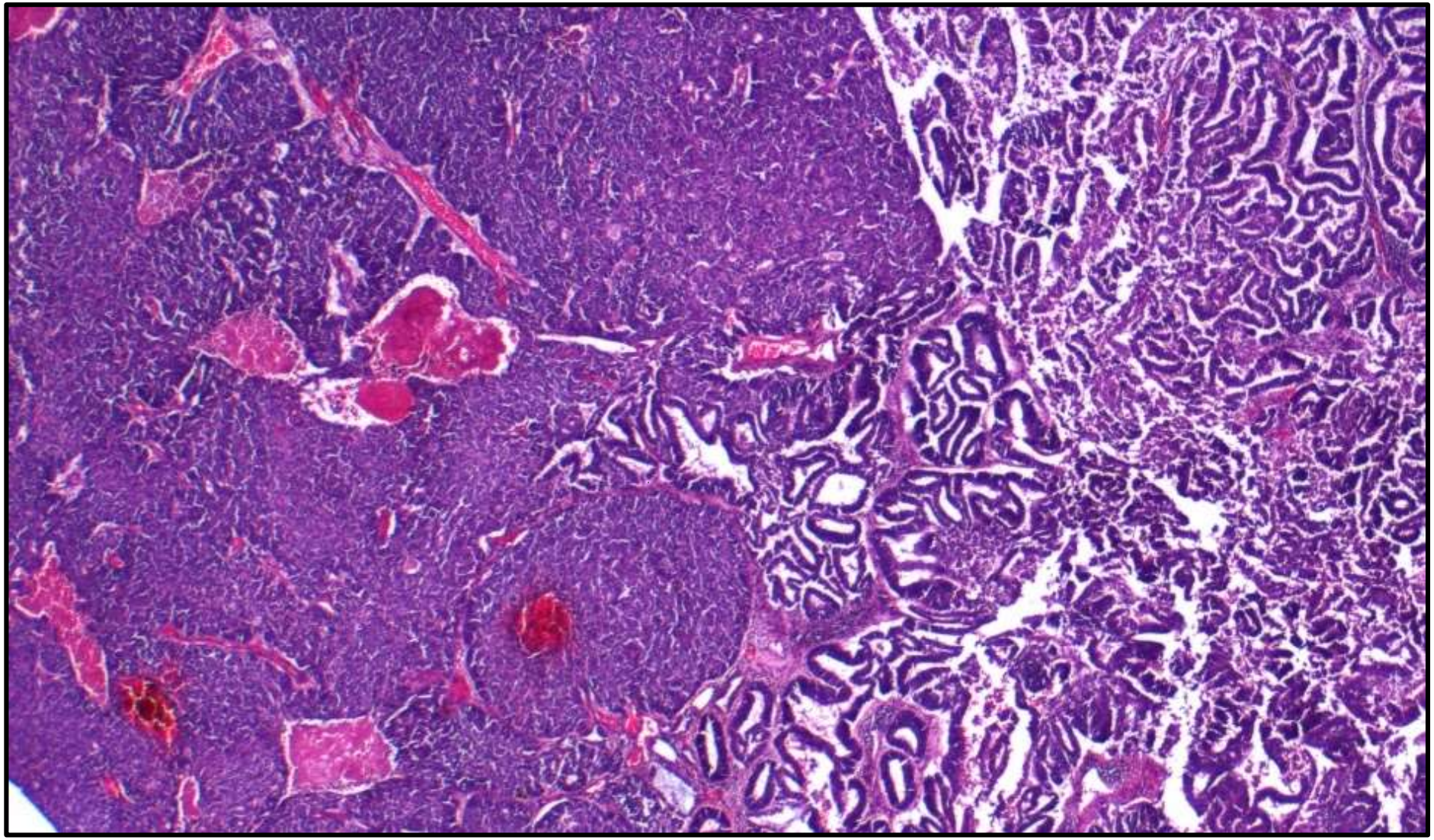




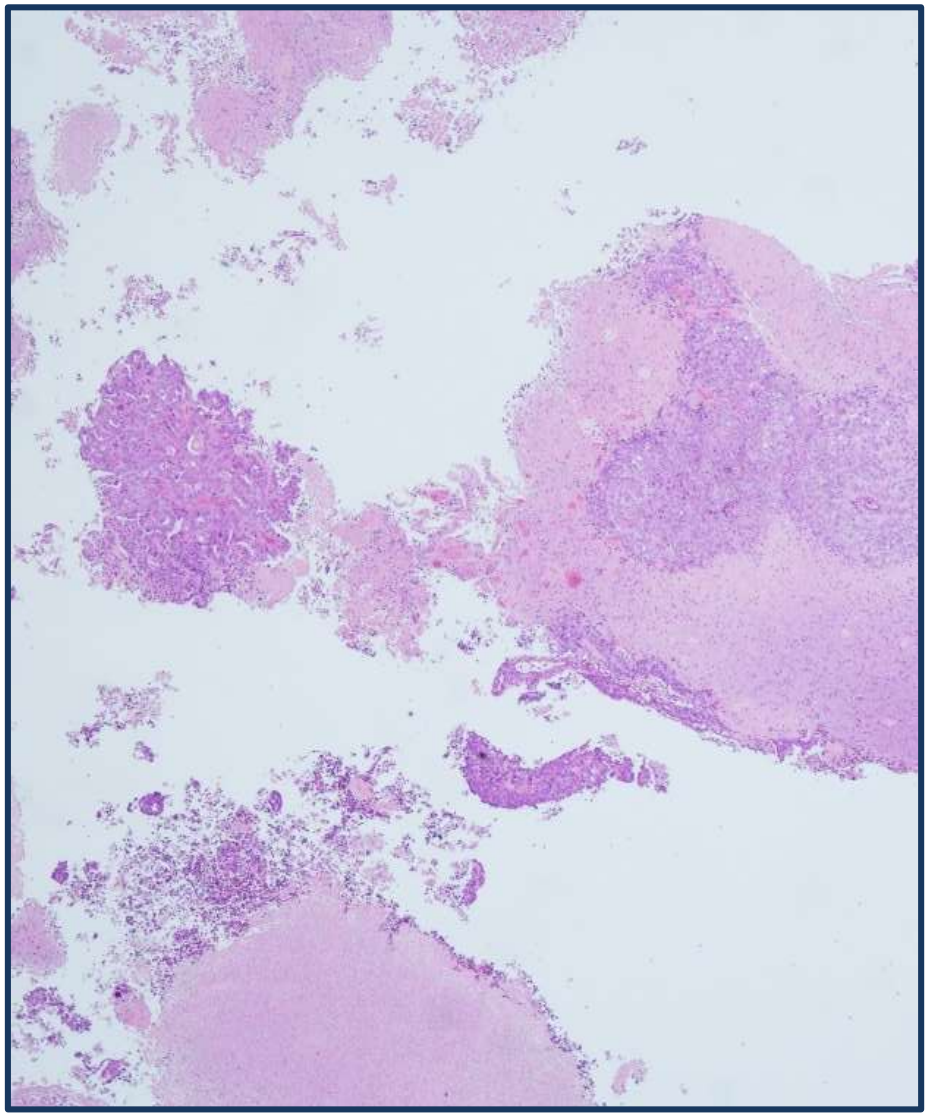
Biopsy issue

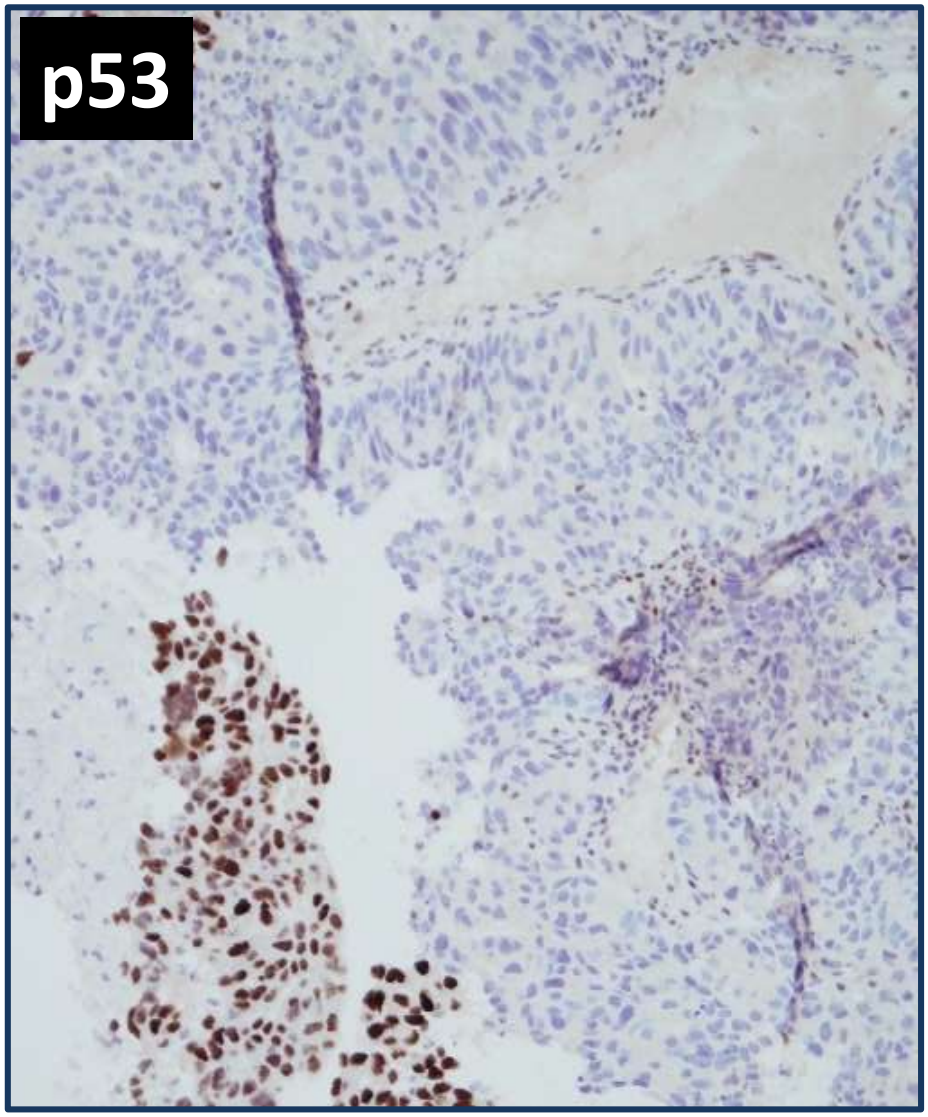
- Tumour heterogeneity

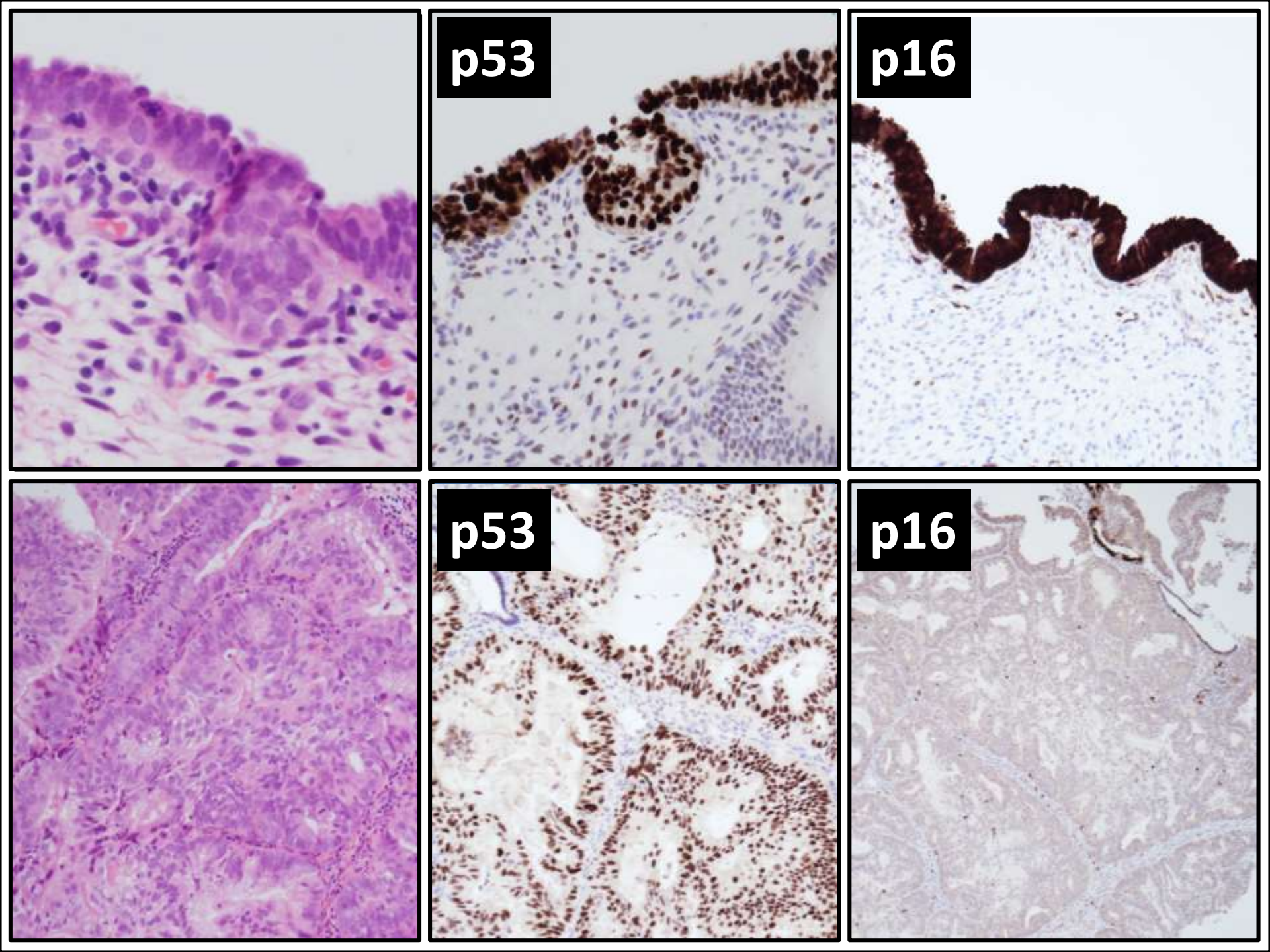
Morphological heterogeneity



Clonal heterogeneity





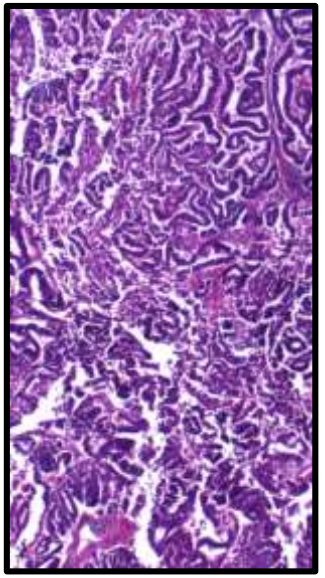

p53
p16
p53
p16

Tumour heterogeneity

- **Tumours are genetically heterogeneous**
  - Each tumour is composed of multiple clones that may have very different outcomes

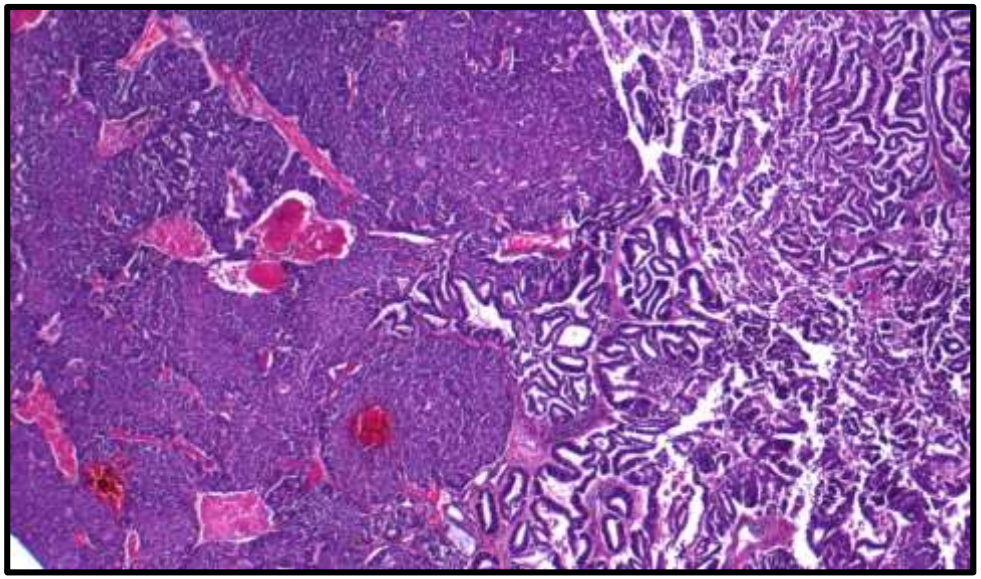
Biopsy limitations

- Tumours are genetically heterogeneous
- **ALL tests can tell us only about the bit of cancer studied**



Biopsy limitations

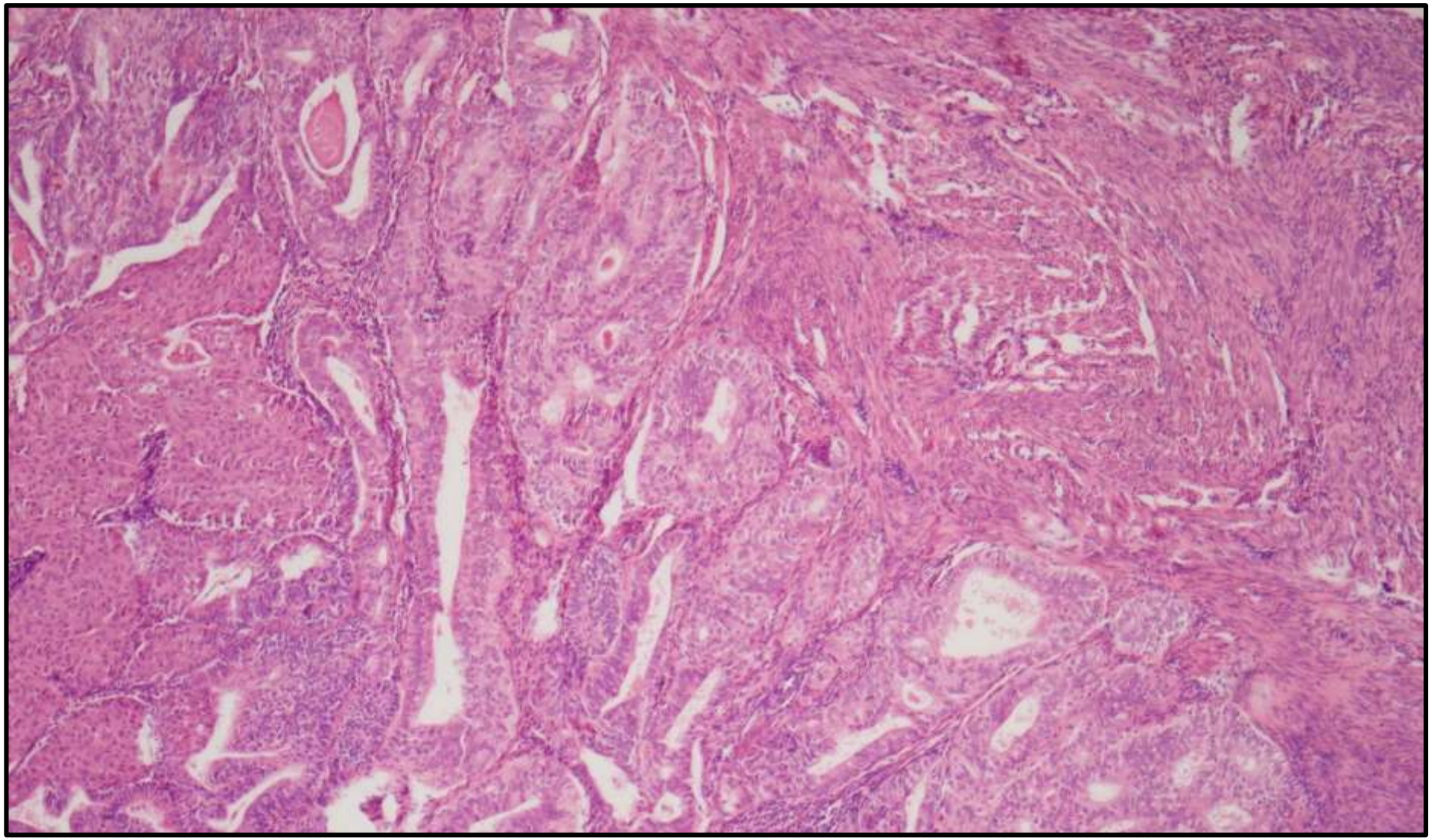
- Tumours are genetically heterogeneous
- **ALL tests can tell us only about the bit of cancer studied**
  - Not about the rest of the tumour



Biopsy limitations

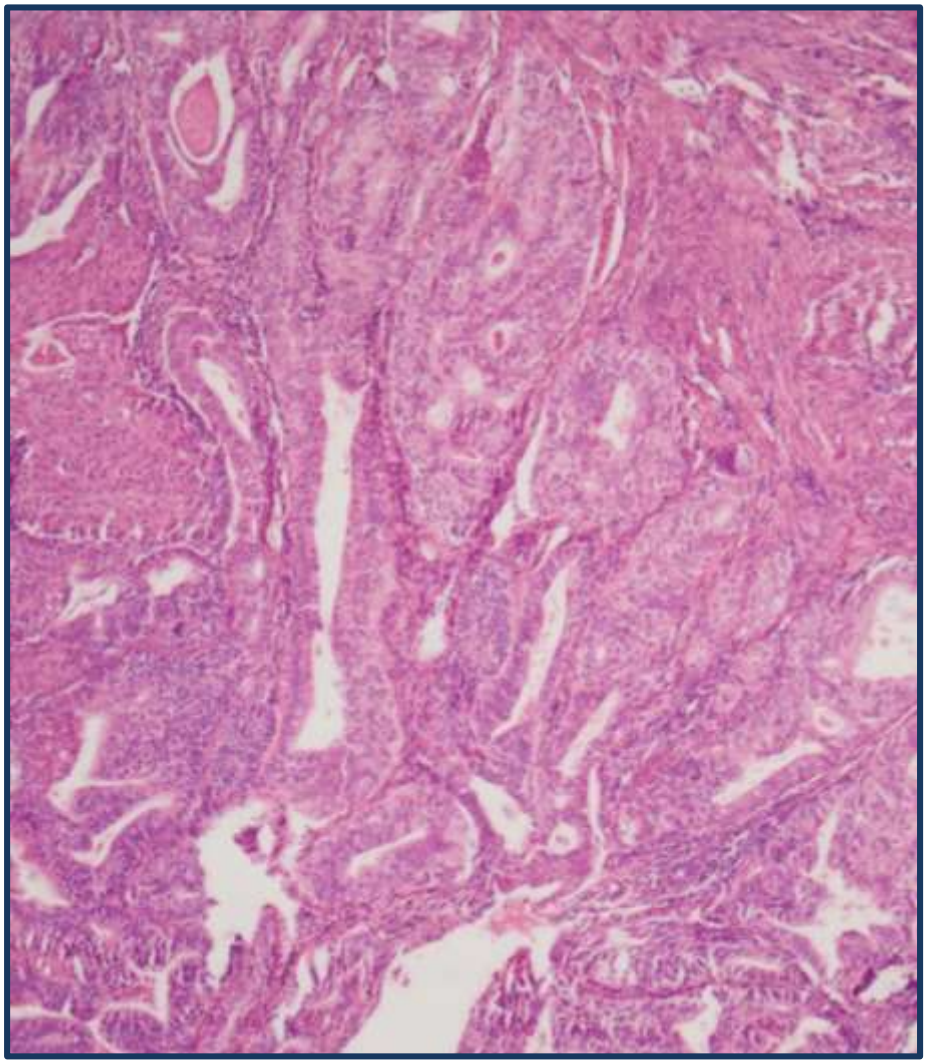
- Tumours are genetically heterogeneous
- **ALL tests can tell us only about the bit of cancer studied**
  - Not about the rest of the tumour
  - Only about **present** morphology and genetic makeup

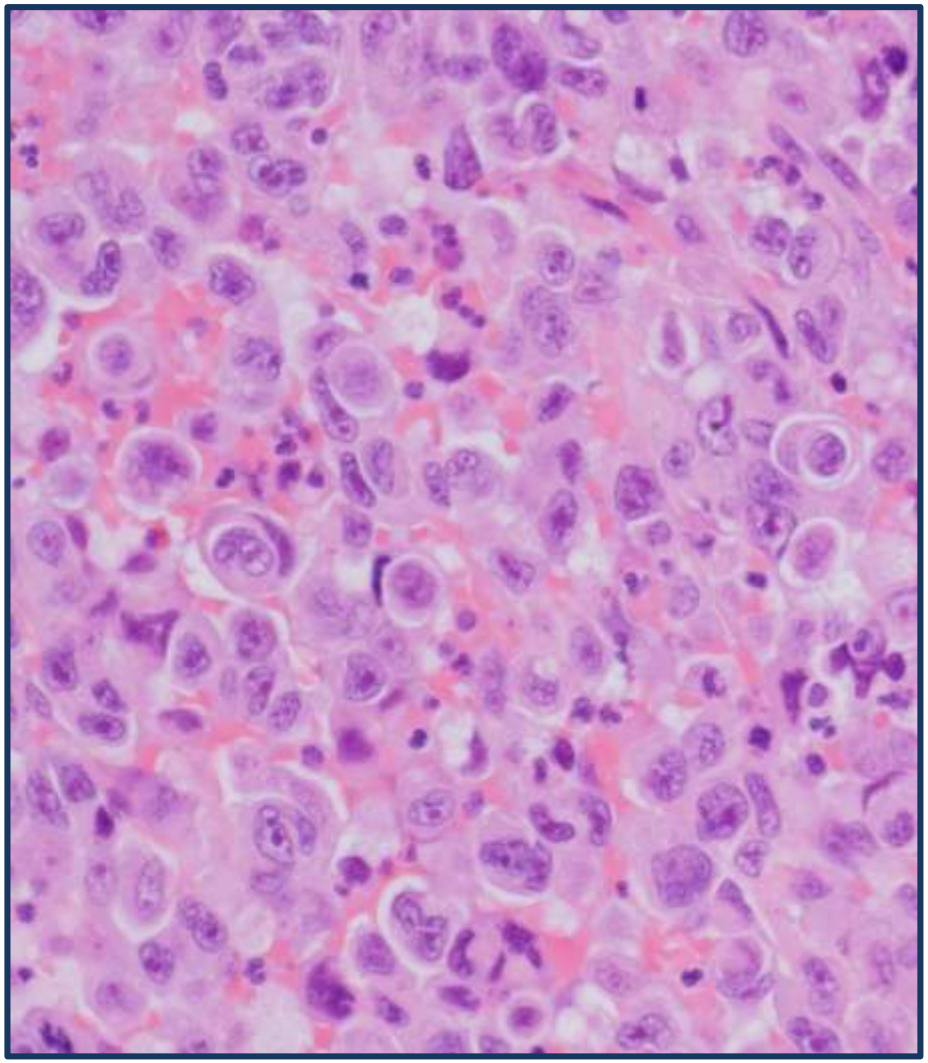
Endometrial cancer hysterectomy



Hysterectomy

Vaginal recurrence 10 yrs later





Biopsy limitations

- Information only about **that part** of tumour at **that time**

Smaller Tissues: Larger Issues

- Interpretation issues
- Sampling issues
- **Time constraints**
- Clinical implications
- Handling issues

Time constraints

- **Bx TAT**
  - Clinically important
  - Cancer targets!
- **Resection TAT**
  - Clinically less urgent – patient has to recover before adjuvant Rx
  - “Clock stopped” after surgery

Smaller Tissues: Larger Issues

- Interpretation issues
- Sampling issues
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- Handling issues

Biopsy vs. resection specimens
Clinical implications

- **Biopsy data guides immediate management**
  - Provides only estimate of grade/extent …
  - But may guide type/extent of surgery

Biopsy vs. resection specimens

Clinical implications

- **Biopsy data guides immediate management**
  - Provides only estimate of grade/extent …
  - But may guide type/extent of surgery
- **Resection data is "The Final Diagnosis"**
  - Definitive data for prognostication and adjuvant therapy

Biopsy pathology
Differences from resection pathology

- **Different clinical requirements**
  - Critical for pathologists to be aware how path data used in that particular case

Bx: Endometrial carcinoma

- **Critical**
  - Low-grade vs. High-grade

Bx: Endometrial carcinoma

- **Critical**
  - Low-grade vs. High-grade
- **Important**
  - G3 EC vs. Serous

Bx: Endometrial carcinoma

- **Critical**
  - Low-grade vs high-grade
- **Important**
  - G3 EC vs. Serous
- **Unimportant**
  - Serous vs. Clear cell vs. Carcinosarcoma

Smaller Tissues: Larger Issues

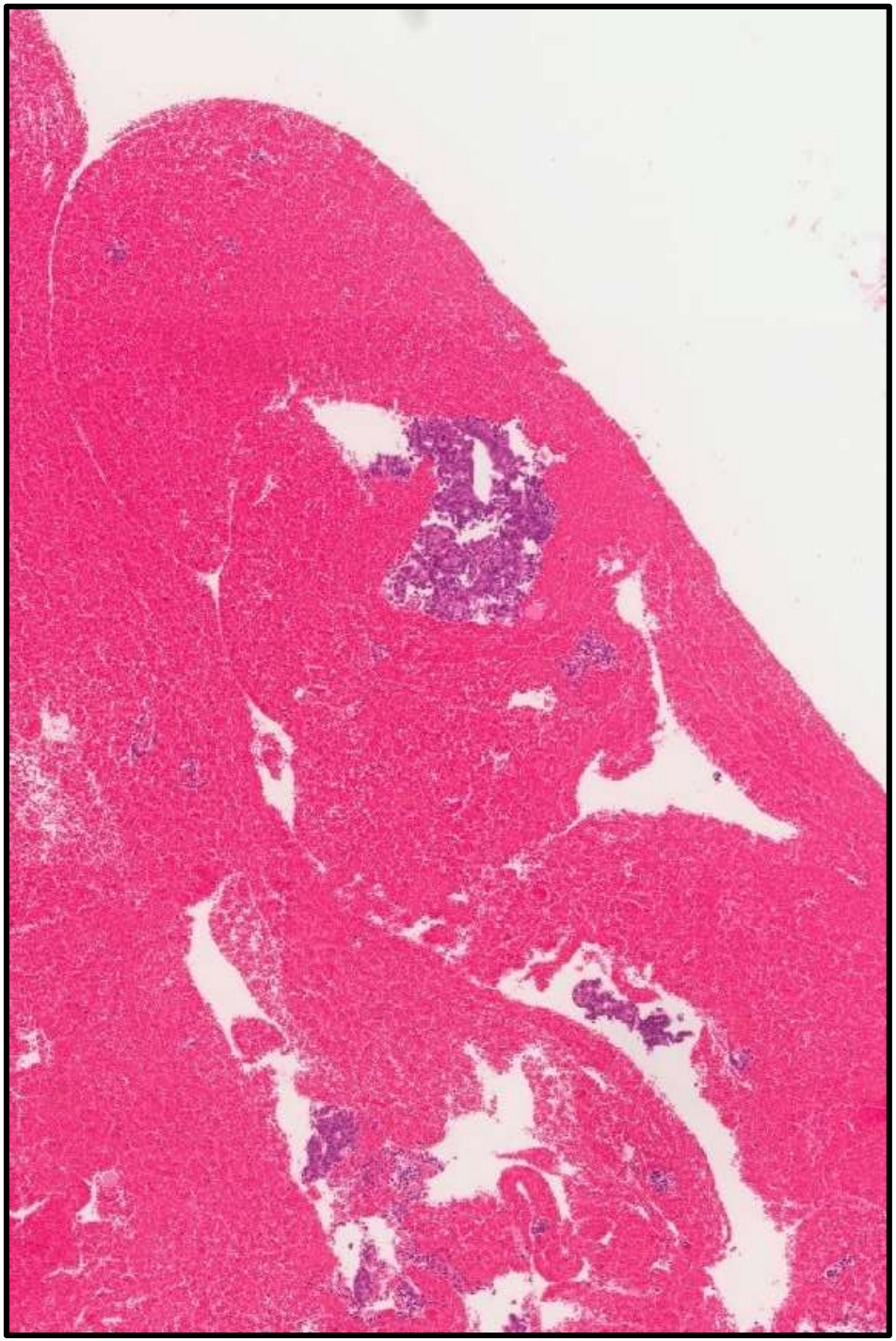
- Interpretation issues
- Sampling issues
- Time constraints
- Clinical implications
- **Handling issues**

Handling biopsies

Cut-up bench

Don’t put too much curettings in each cassette

- Fragments in deeper level may be from different part of endometrium

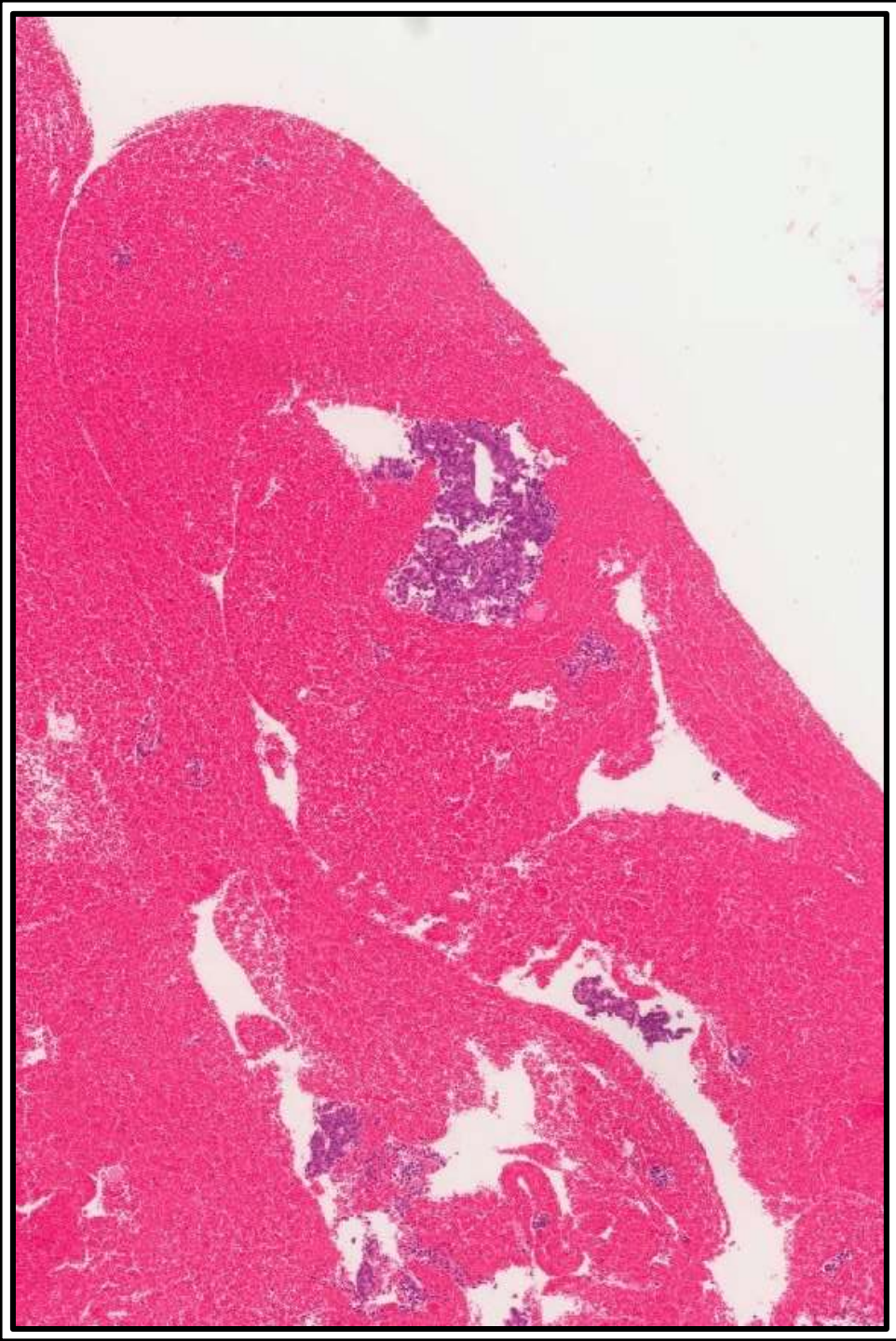


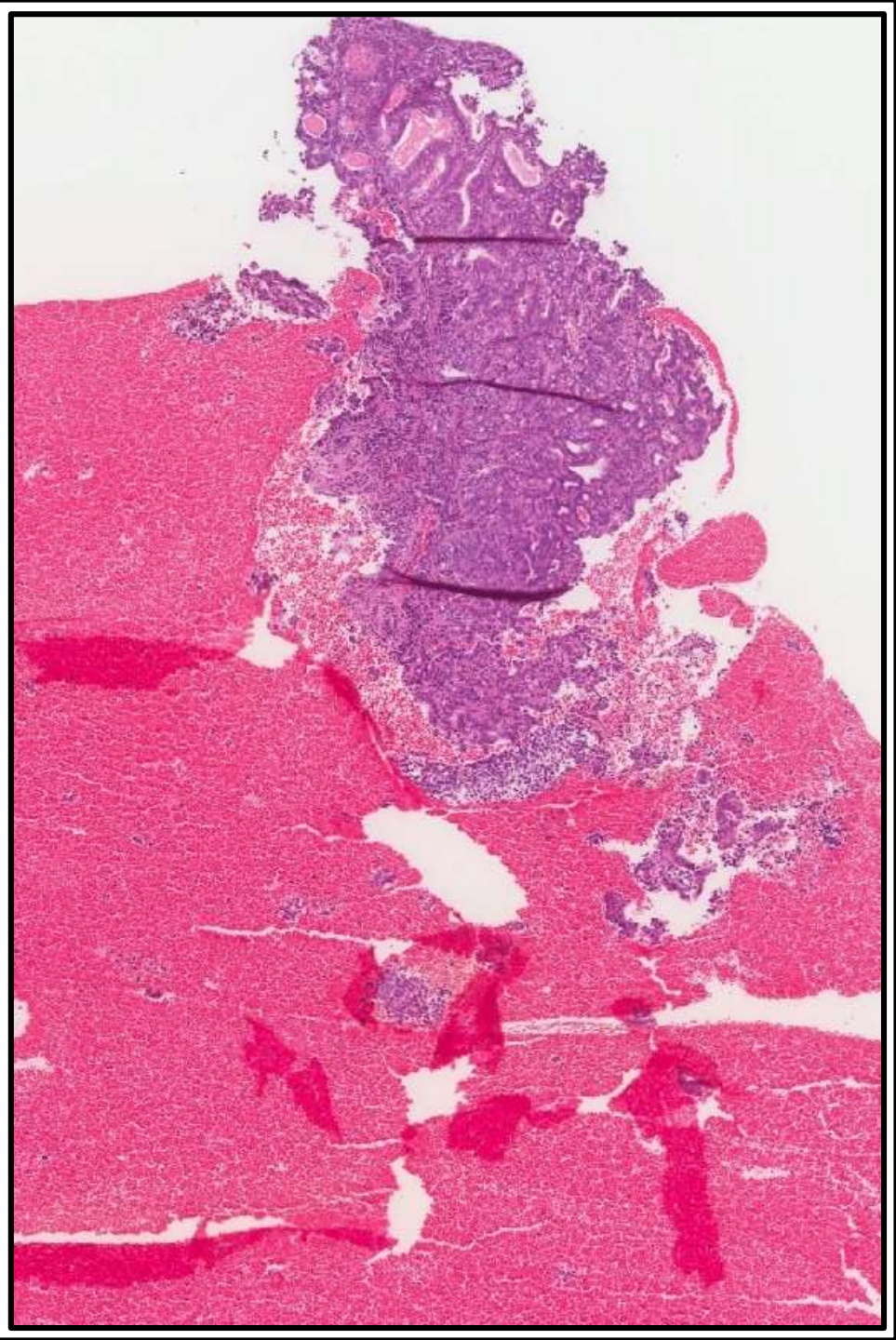
Biopsy pathology
Differences from resection pathology

- **Less tissue for morphology/IHC**
  - Taking extra blocks not an option

Biopsy pathology
Differences from resection pathology

- **Less tissue for morphology/IHC**
  - Taking extra blocks not an option
    - However, deeper levels is an option





Handling biopsies
Cut-up bench

- Don’t put too much curettings in each cassette
  - Fragments in deeper level may be from different part of endometrium
- **Consider embedding core biopsies in multiple cassettes**

Core biopsy handling

Core biopsy handling

Handling biopsies

Cut-up bench: Macro

Handling biopsies

Cut-up bench: Macro

- **Must record number of pieces in each block (esp when <5):** Request levels if fewer in block
- **Max. dimension of each (or range) is sufficient**
  - No need to measure each bx in 3 dimensions
  - Only 2 dimensions seen on slide
- **Detailed macroscopic description (colour, consistency etc) is of limited clinical value**

Handling biopsies

Cut-up bench: Macro

MACRO:
Mole, neck. Two skin shaves the largest measuring 10 x 5 x 2 mm with a grey surface smaller piece measuring 6 x 4 x 2 mm with a grey surface, larger piece sliced in to three. A1, AE.

Fixation issue

- Formalin ***permeation time*** is 1mm/hour
- Tissue does ***NOT*** fix at 1mm/hr
- Fixation requires cross linking of proteins
- Cross-linking of proteins takes much longer
- Optimal fixation: 8 – 24 hours

Fixation issue

- **Small biopsies may need as long fixation time as larger tissue blocks**

Fixation issue

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  - Recent study suggests that shorter fixation time may not affect ER immunostaining

Fixation issue

- **Small biopsies may need as long fixation time as larger tissue blocks**
  - Recent study suggests that shorter fixation time may not affect ER immunostaining
- **Under-fixation causes more problems than over-fixation**

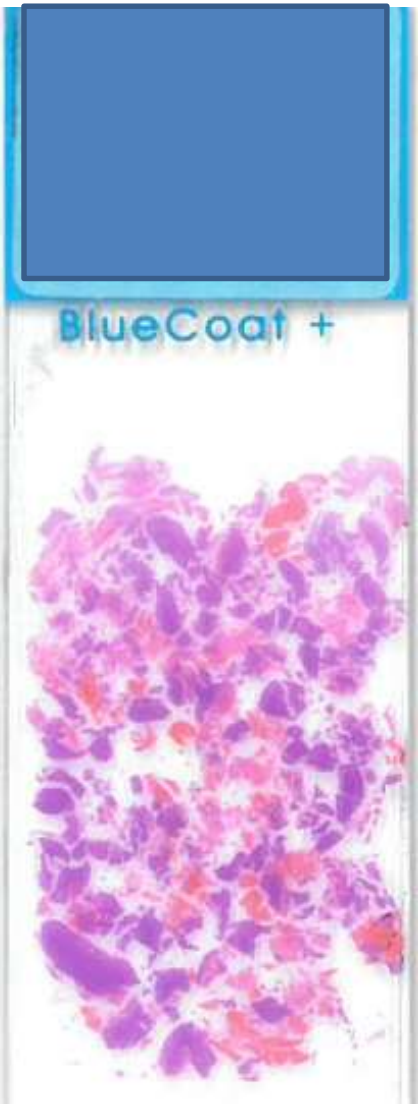
Reporting biopsies
Immunohistochemistry

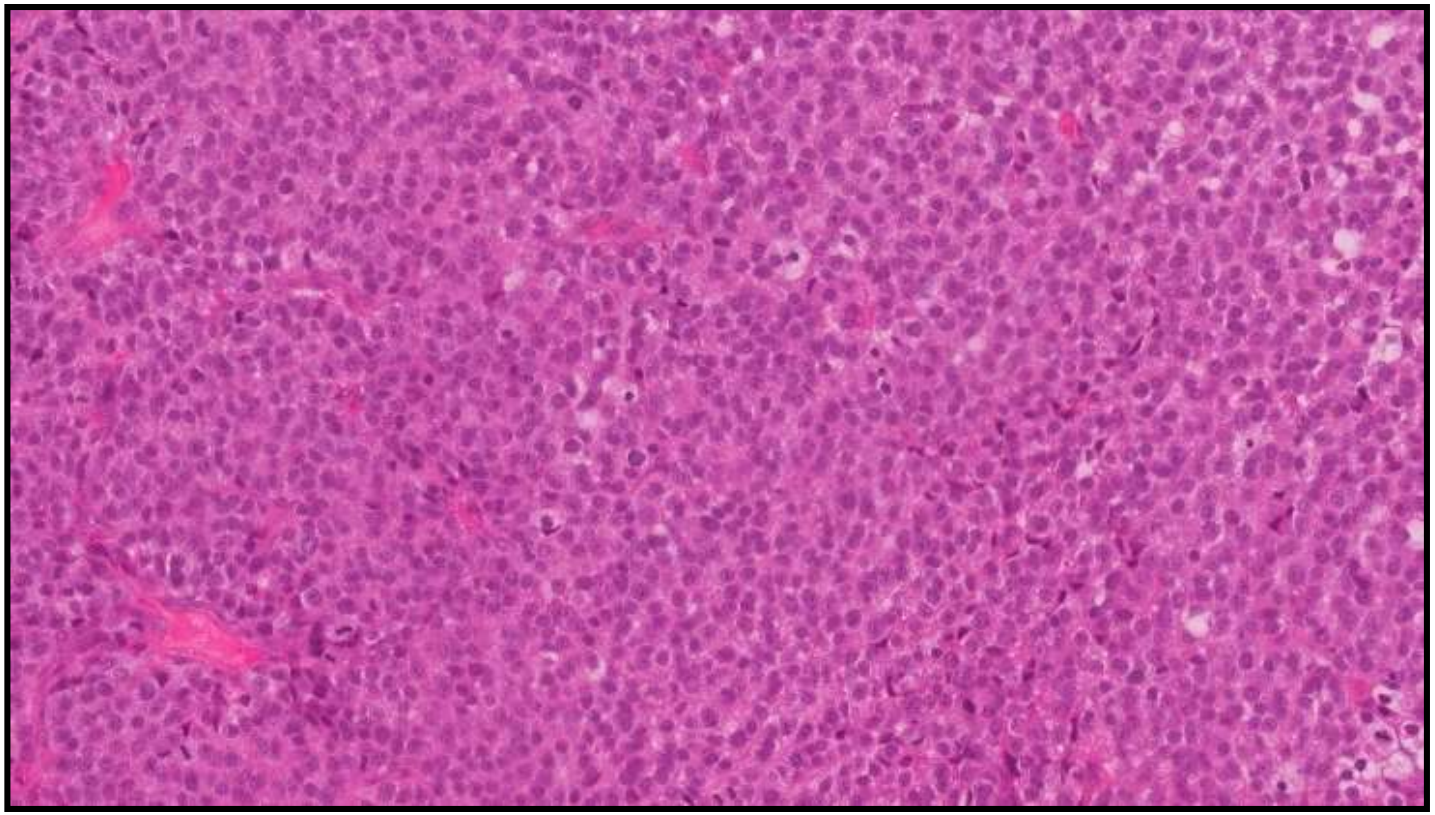
- **Blunderbuss approach not recommended**
  - Wasteful
  - Often yields confusing results
  - May exhaust tissue

Reporting biopsies
Immunohistochemistry

- Blunderbuss approach not recommended
- **Size of immunopanel should depend on:**
  - Clinical scenario
  - Morphological differential diagnosis
  - Degree of uncertainty
  - Significance of differential diagnosis

Handling





Reporting biopsies
Immunohistochemistry

- If multiple immunostains likely then consider melting block and dividing material into multiple blocks

Core biopsy handling
Immunohistochemistry

- **Option A**
  - Serial or deeper sections cut upfront
  - H&E on first and last section
  - Rest retained for immunohistochemistry
    - Only 1 spare on each slide to avoid tissue waste
- **Option B**
  - 1 section with minimum trimming
  - If non-diagnostic:
    - 3 levels + immuno spares based on DD

Reporting biopsies
Immunohistochemistry

- **Try not to exhaust block**
  - Retain some material for IHC/molecular testing in future (may be several years later)

Thank You