The British Association of Gynaecological Pathologists

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Lecturer – Dr Trupti Mandalia

Trupti is a Consultant Histopathologist at Royal Devon University Hospital. She serves as the Lead Gynaecological Pathologist and Lead Cervical Screening Pathologist and is currently the Deputy Organiser of the National Gynaecological Pathology EQA.
She is passionate about teaching and has delivered numerous local, regional, and national educational sessions over the past 16 years.

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Basic Cervical Histopathology Course

- Title: Squamous cell carcinoma including measurements
- Speaker: Trupti Mandalia
- Affiliation: Royal Devon University Hospital NHS Trust
- Date : 4th February 2026

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Speaker disclosures

Choose one

- ❑ I have no financial conflicts of interest to disclose

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Squamous Cell carcinoma, including measurements

Dr Trupti Mandalia
Royal Devon University Hospital NHS Trust
Exeter

Outline

- Introduction
- Morphological features of invasion and common diagnostic challenges
- Classification and grading of SCC
- FIGO 2018 staging
- Tumour measurements

Squamous Cell Carcinoma

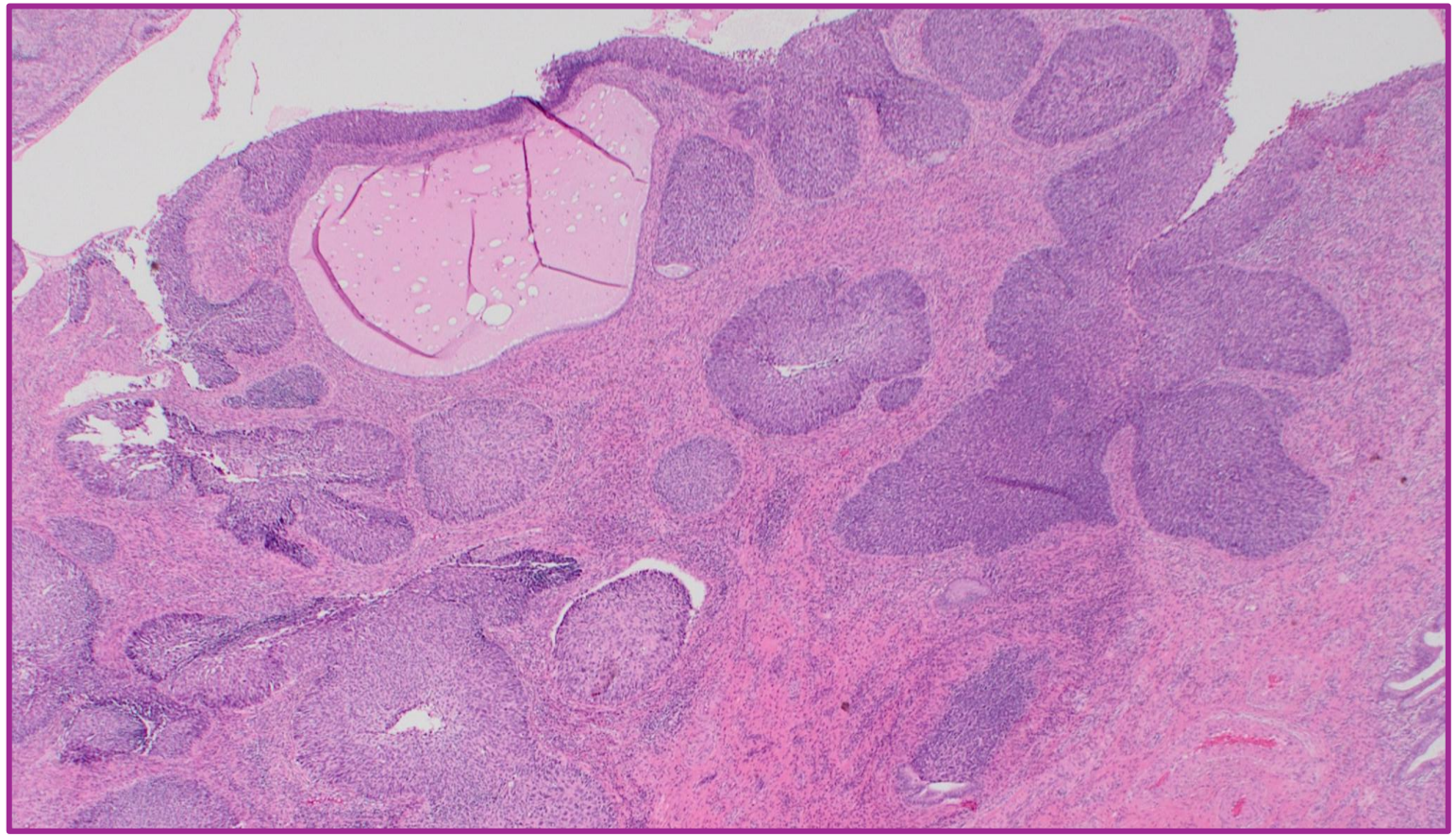
- Most common subtype of cervical carcinoma
- 80 to 90% of cervical carcinoma
- Majority are HPV driven (HPV 16 and HPV 18 most common high risk genotypes responsible)

HIGH RISK HPV genotypes

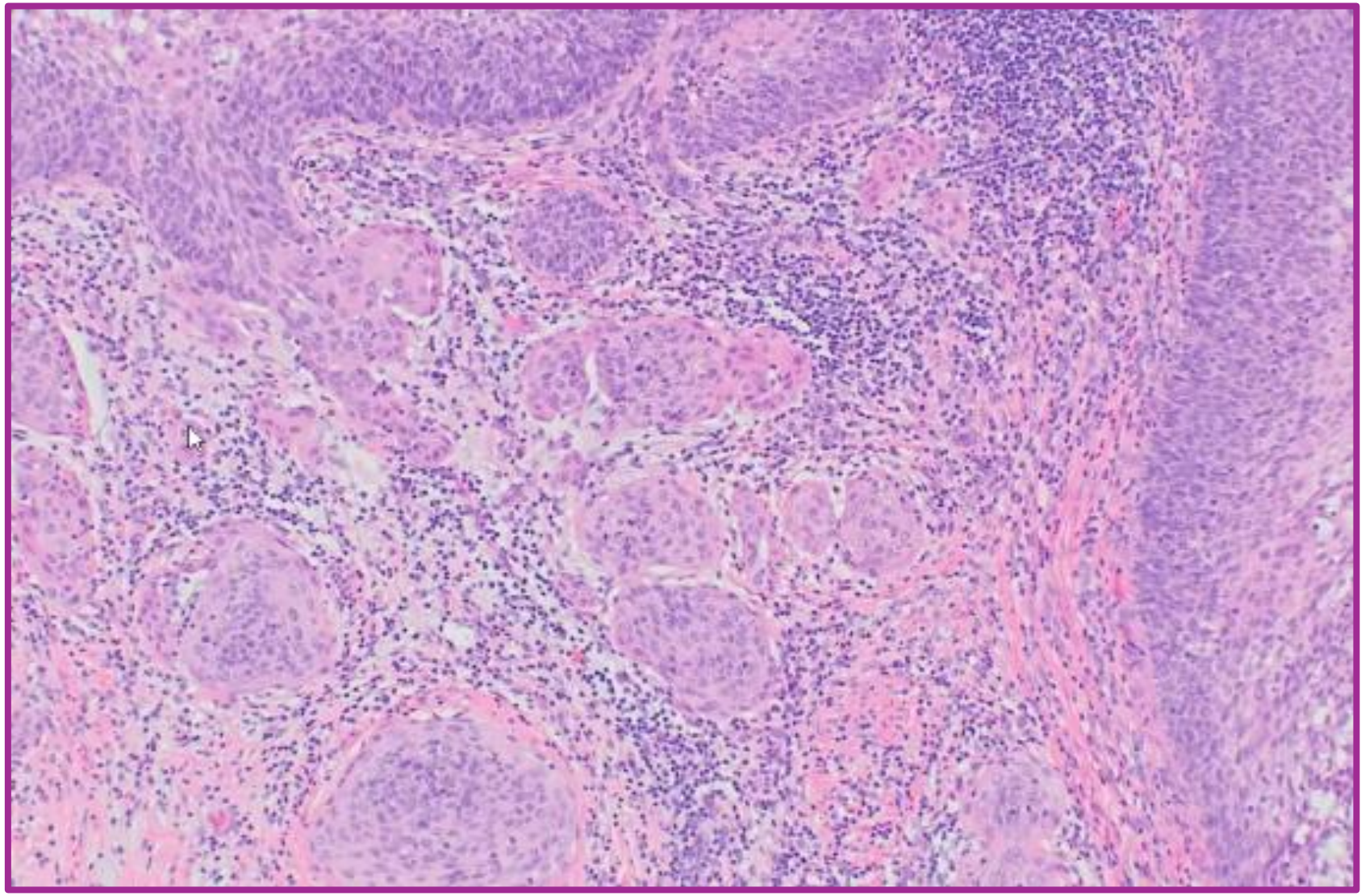
Risk Category	HPV Subtypes	Approx. Contribution
VERY HIGH RISK	**HPV 16, 18**	70-75%
HIGH RISK	HPV 31, 33, 45	15–20%
INTERMEDIATE RISK	HPV 52, 58, 35, 39, 51, 56, 59	10–15%

Persistent infection with high risk HPV is the principal etiological factor in the development of cervical cancer.

Squamous cell carcinoma- precursor lesion



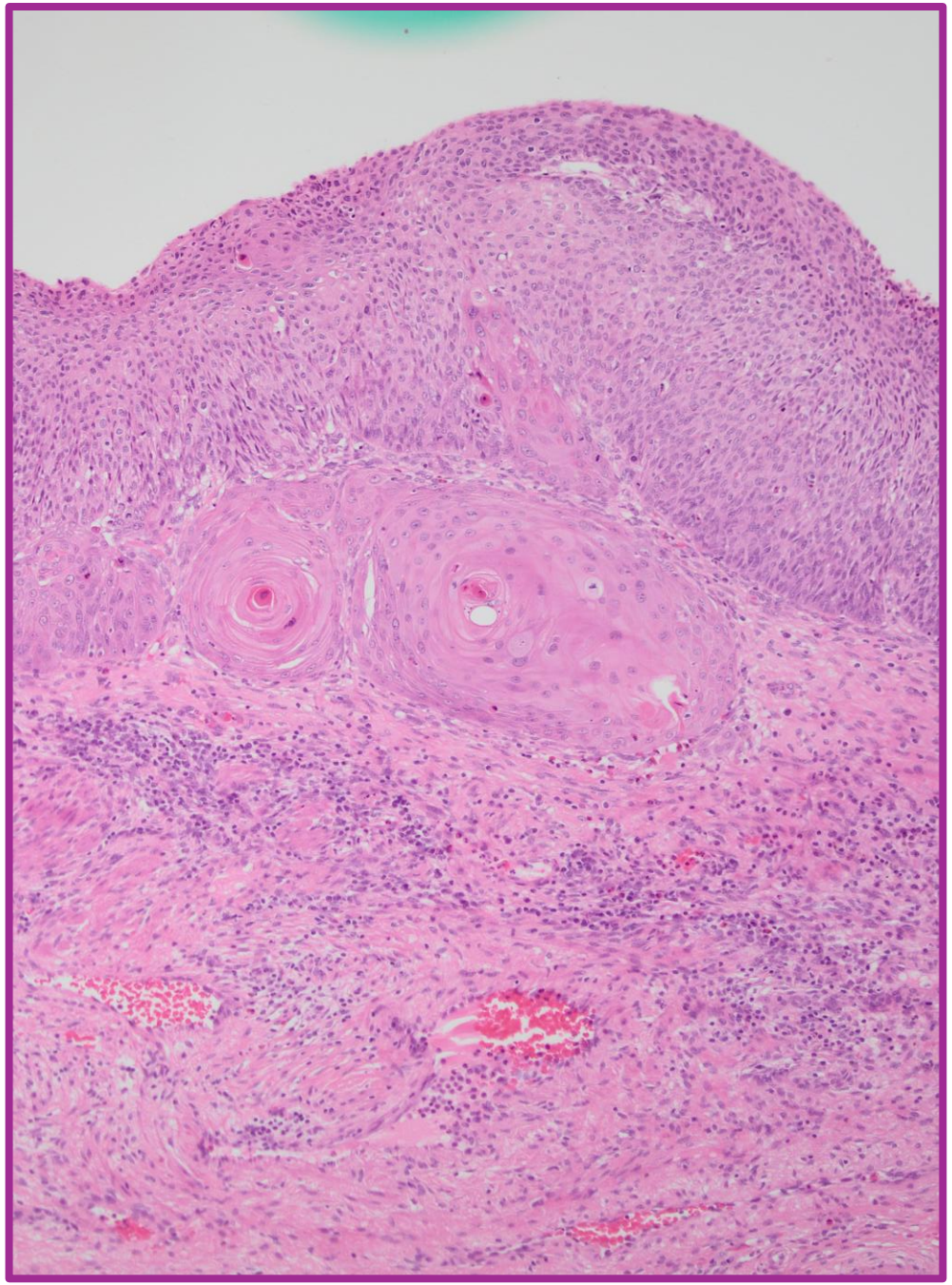
Diagnosis of Invasion

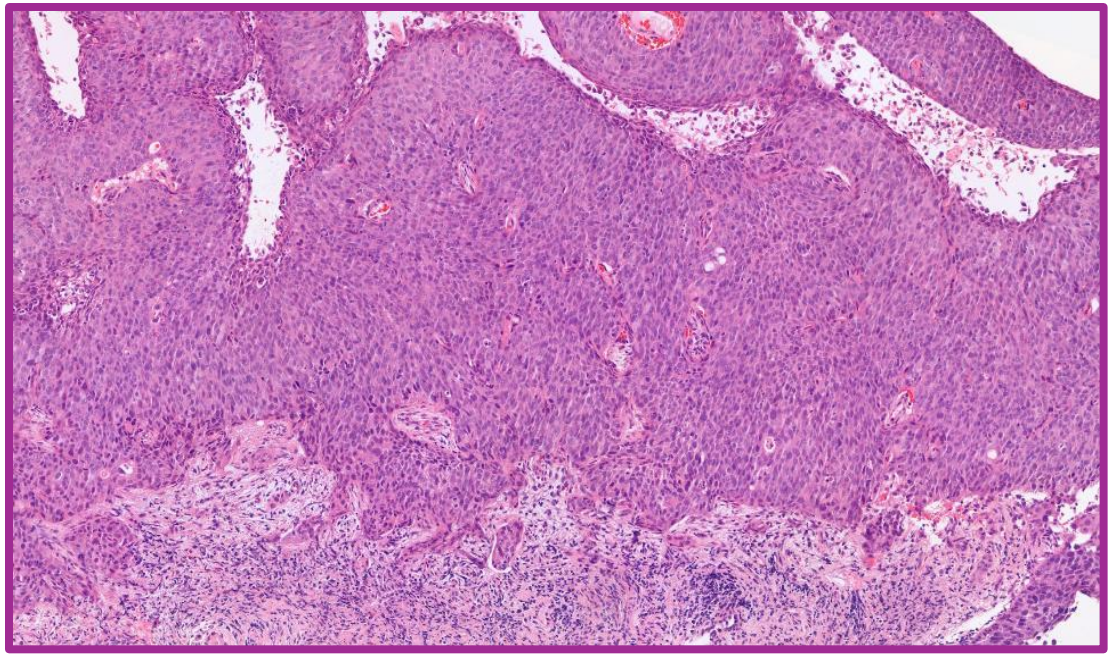


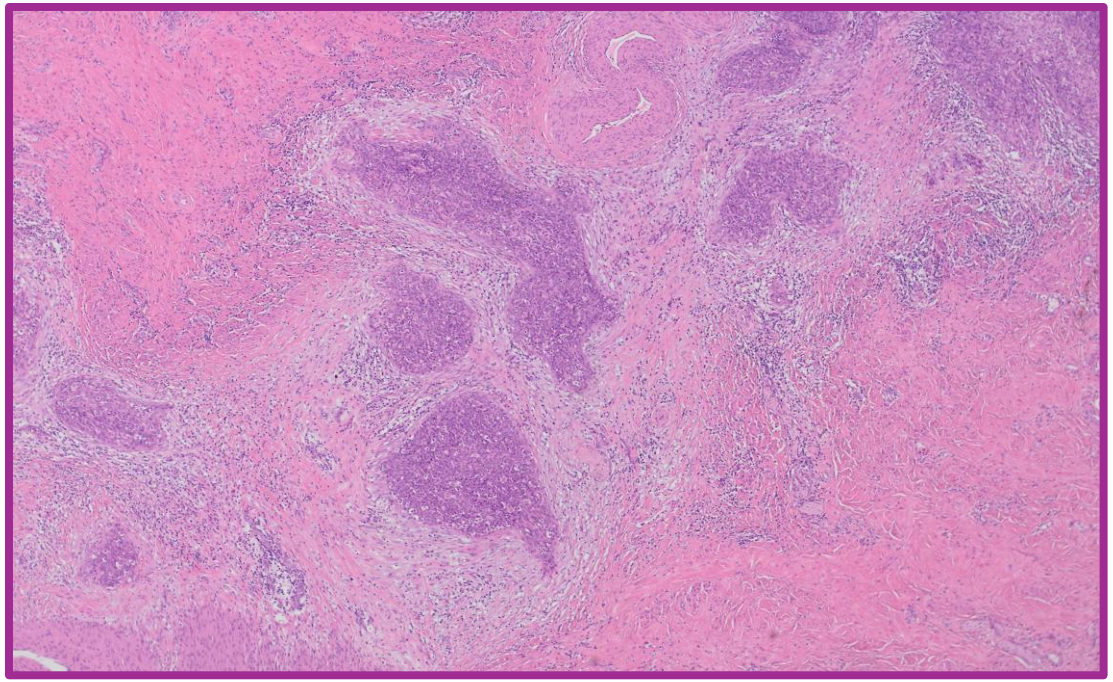
Prof Andre Pinto(Isgyp webinar)

Diagnosis of Invasion

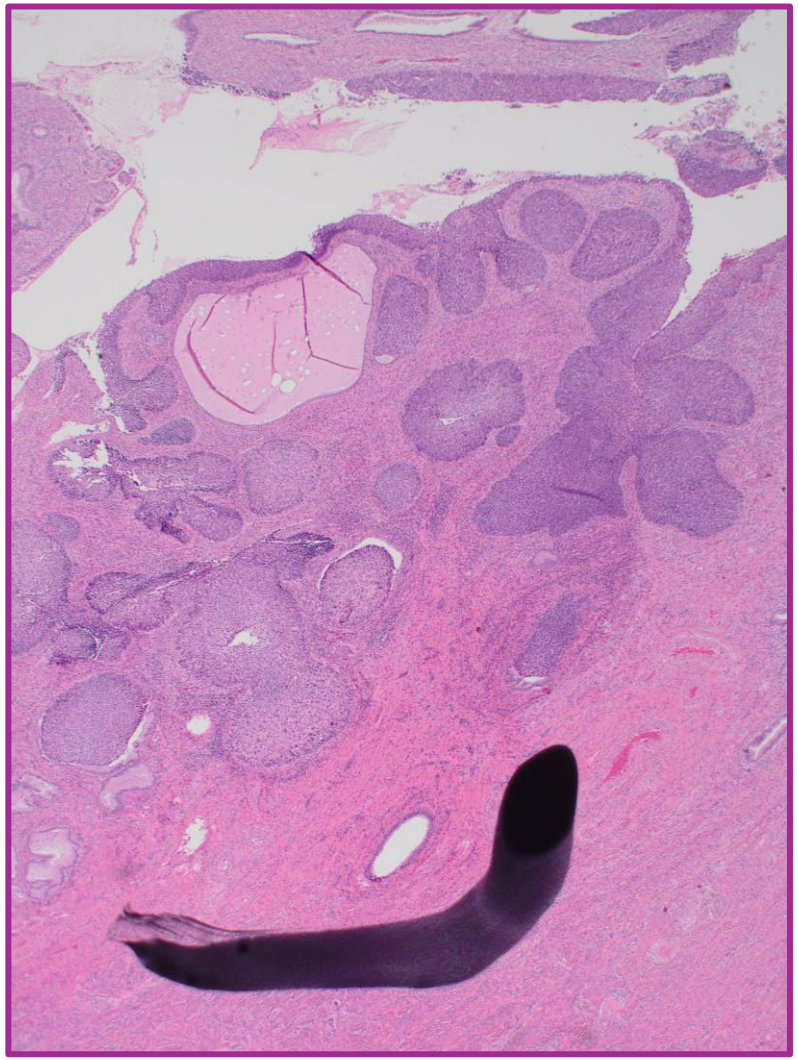
- Irregular epithelial stromal junction
- Inflammatory reaction
- Irregular tongues/buds extending into the stroma
- Loss of polarity and basal palisading
- Stromal reaction (loosening/desmoplasia)
- Paradoxical maturation

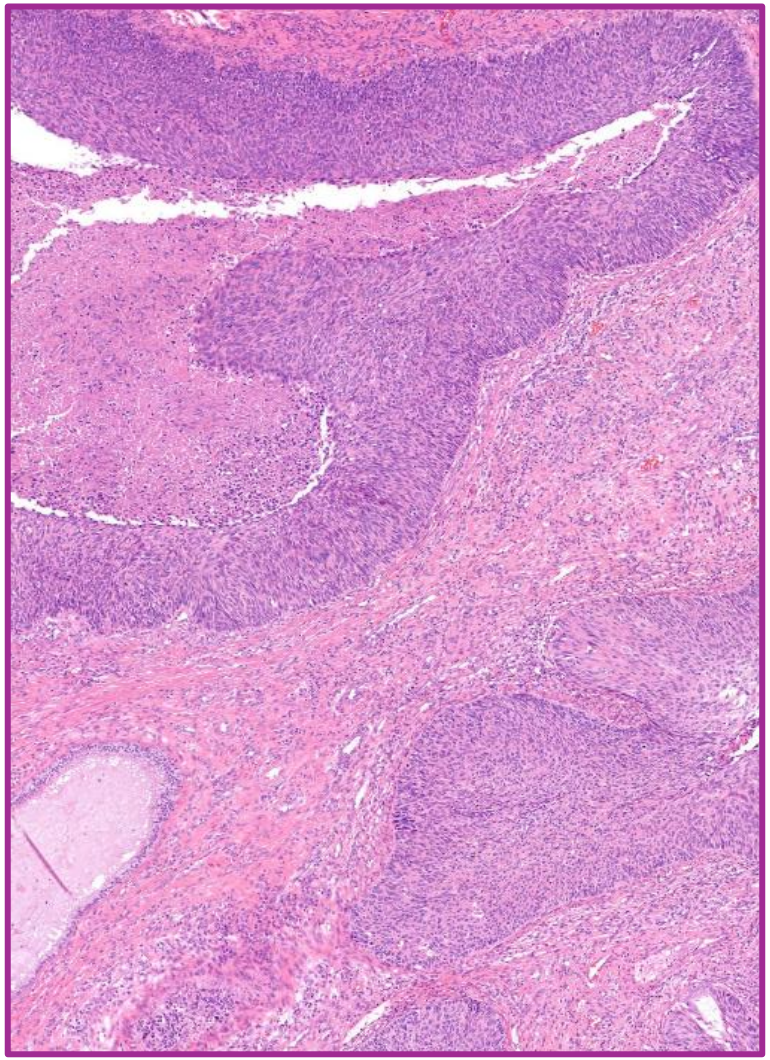






Expansile crypt involvement – Aggressive CIN3

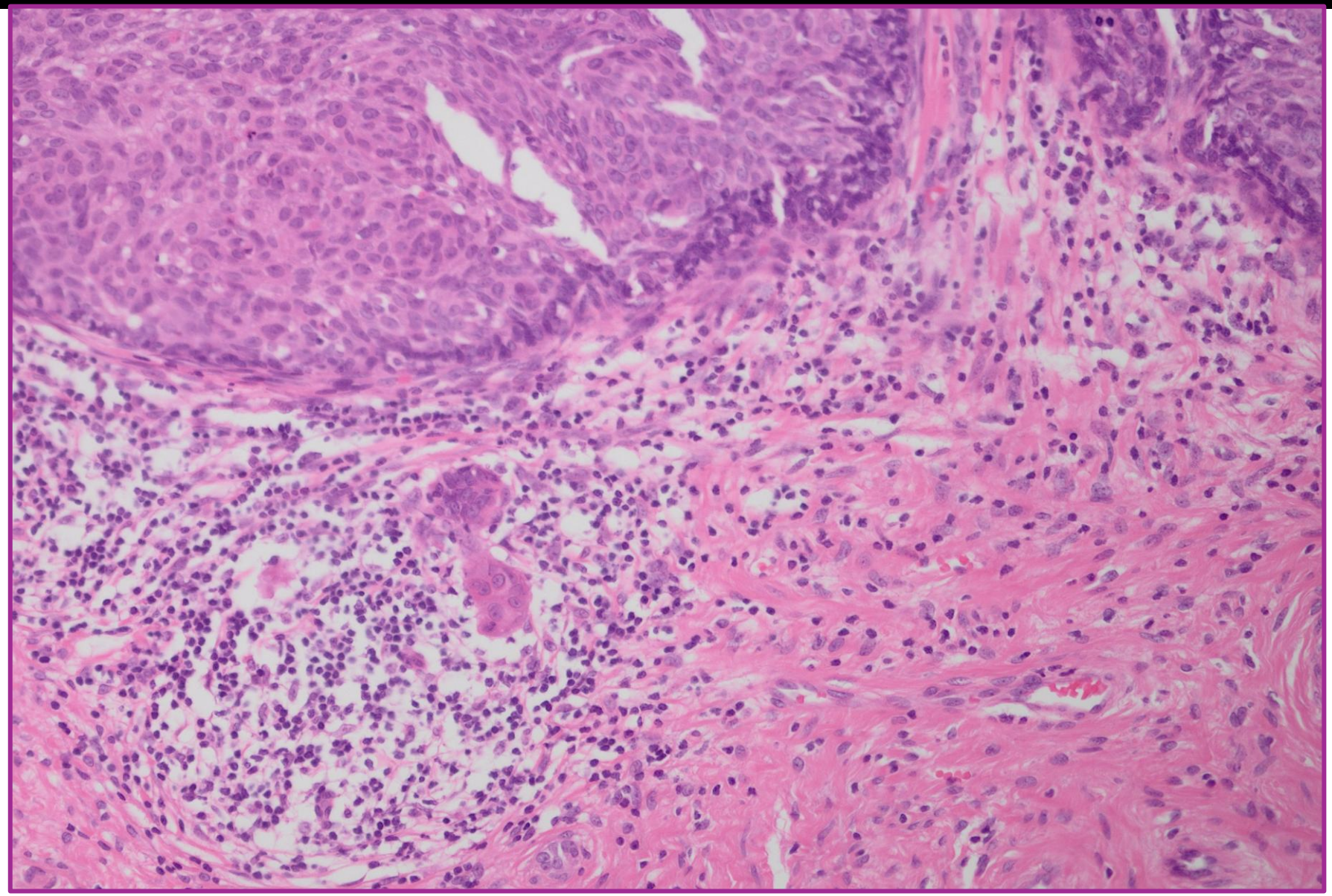


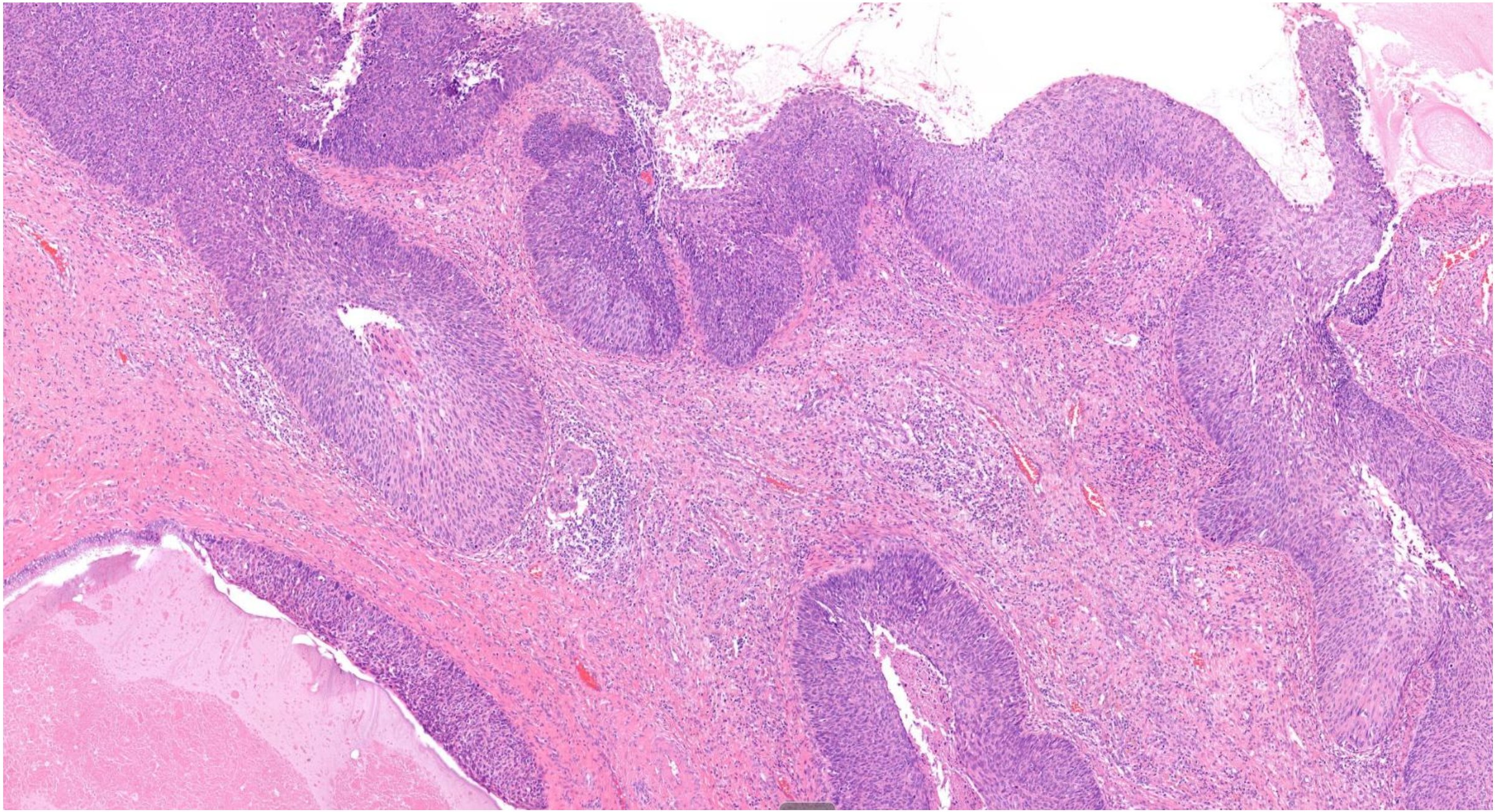


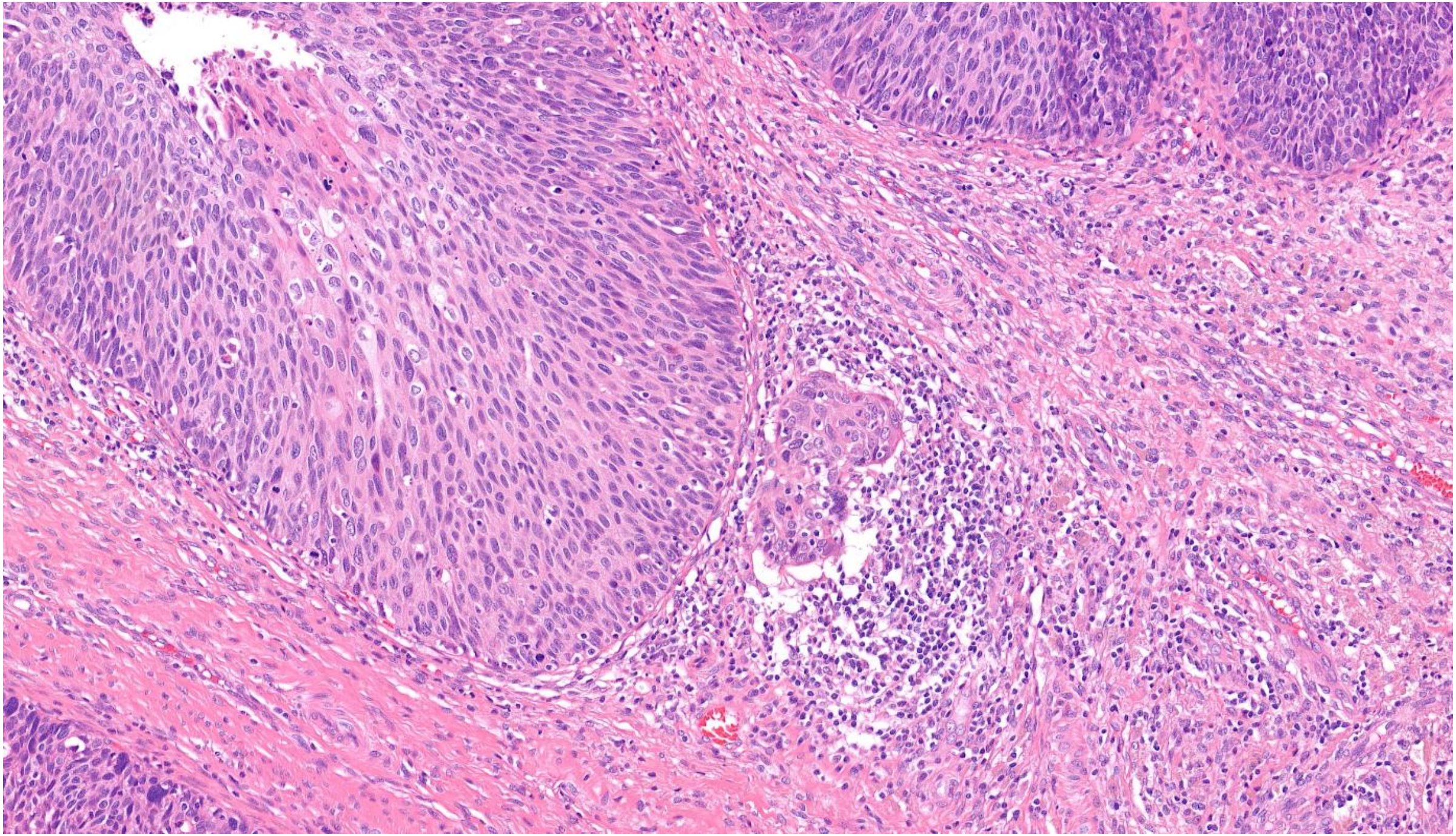
- Extensive involvement of surface epithelium
- Expansion of crypts
- luminal necrosis
- Keratinous debris
- Pericryptal fibroplasia and inflammation,

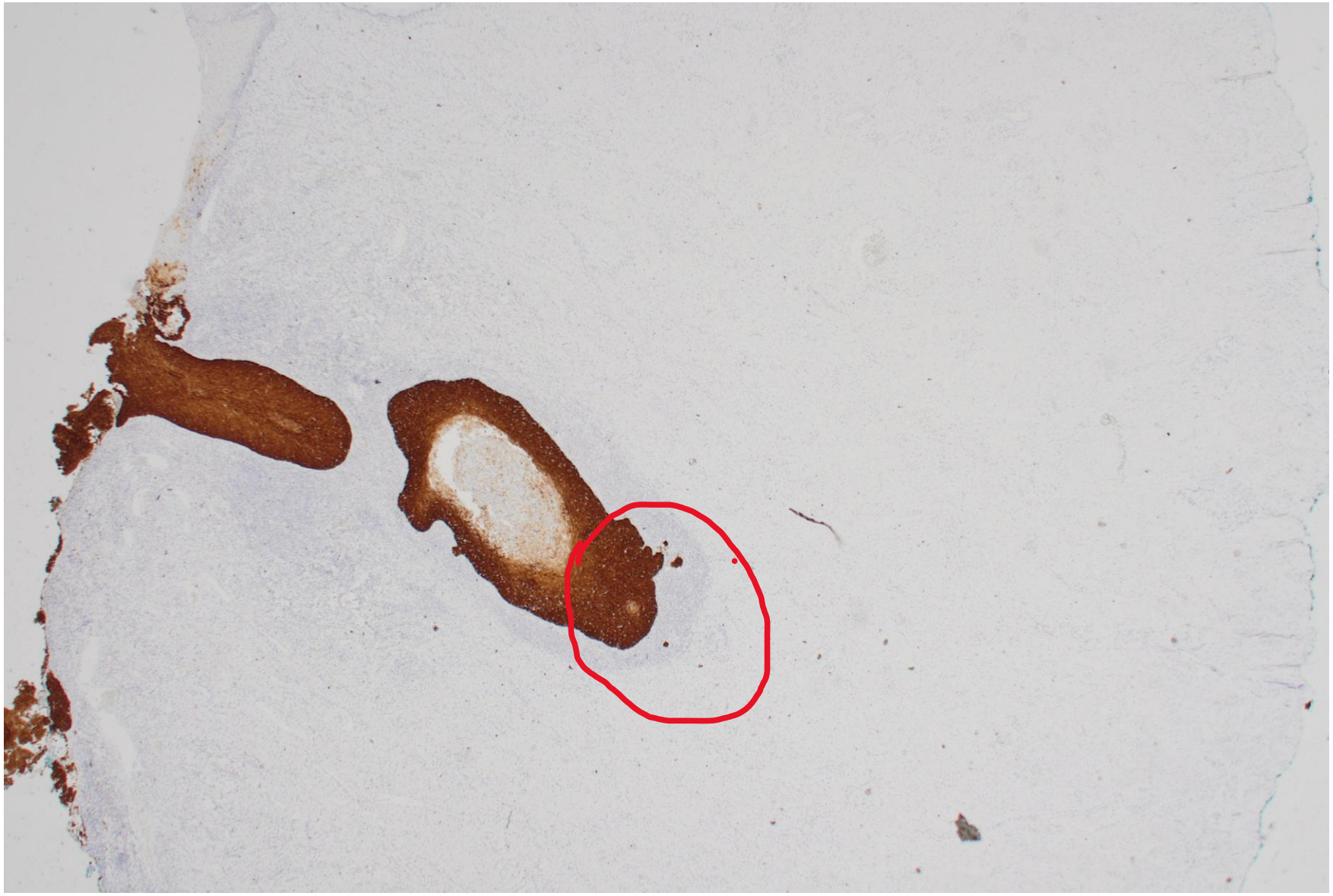
Do multiple levels

EARLY STROMAL INVASION

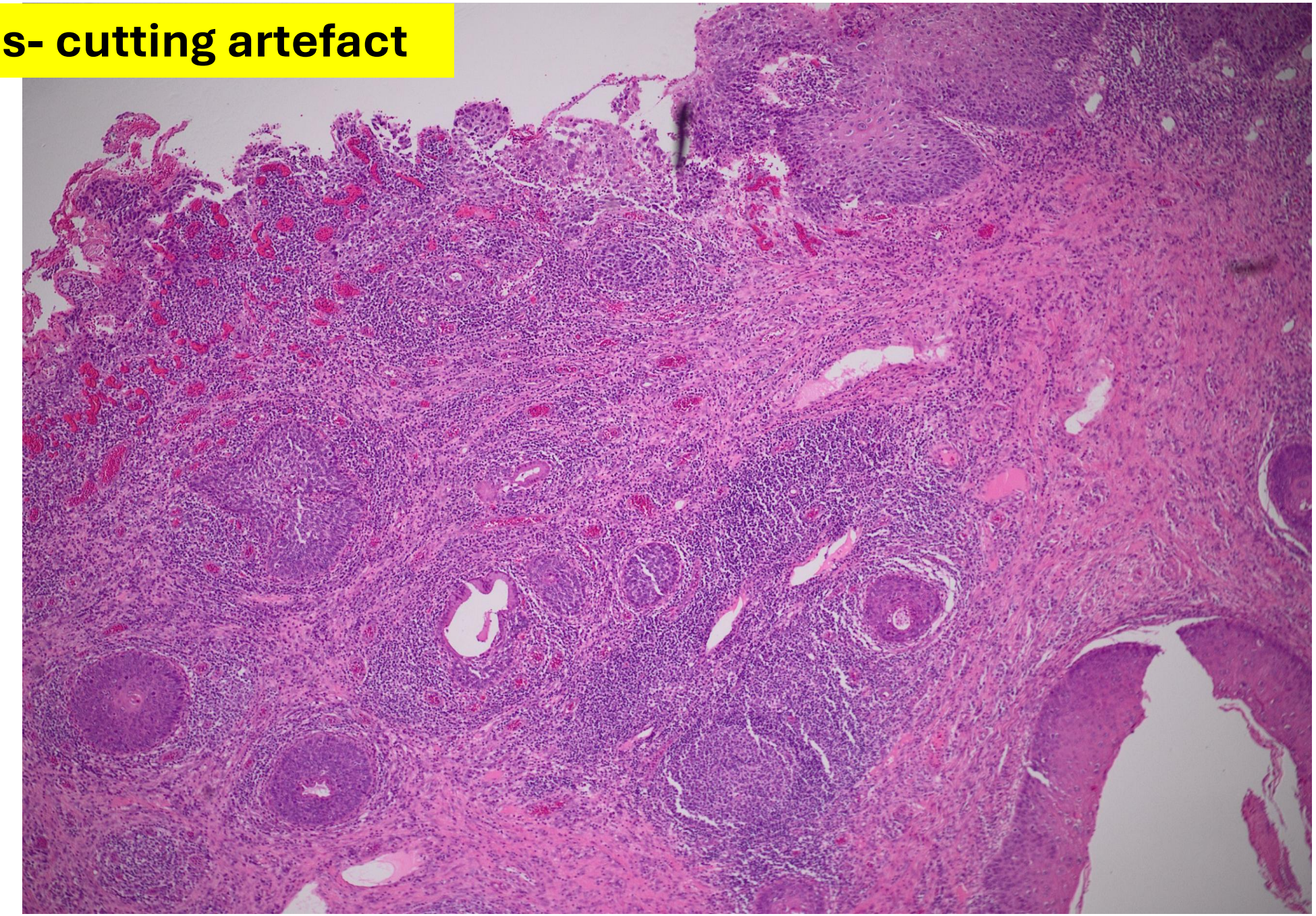




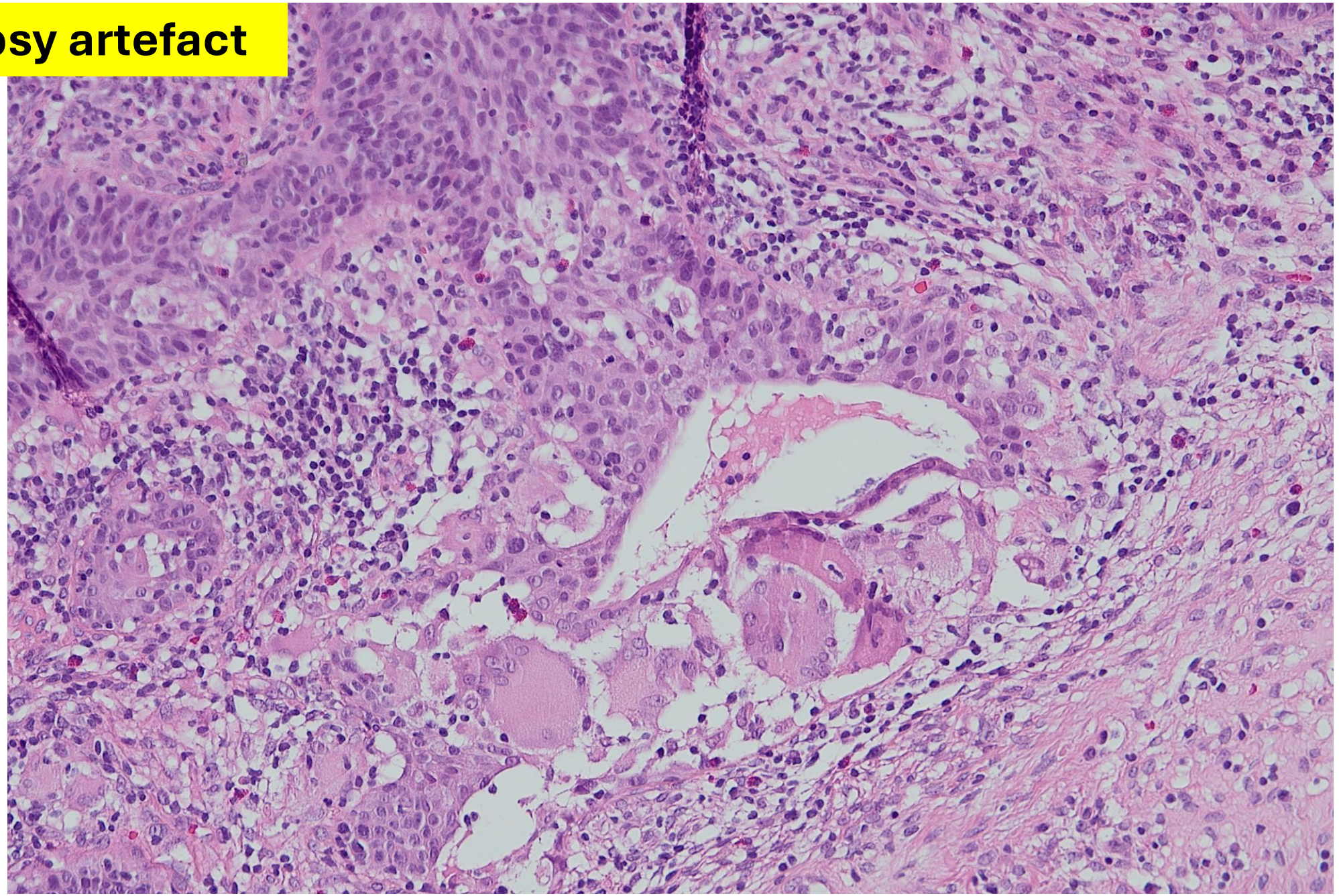


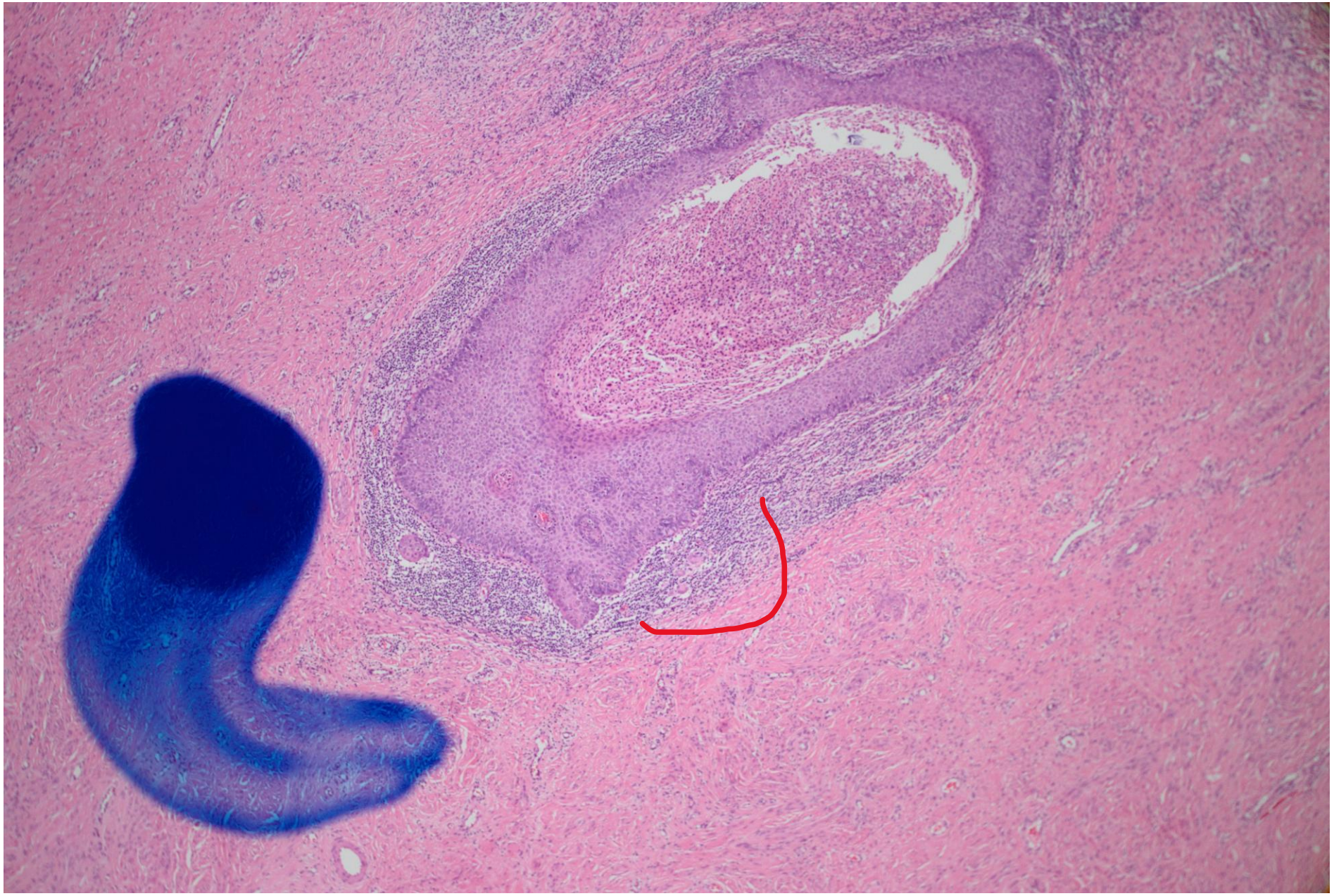


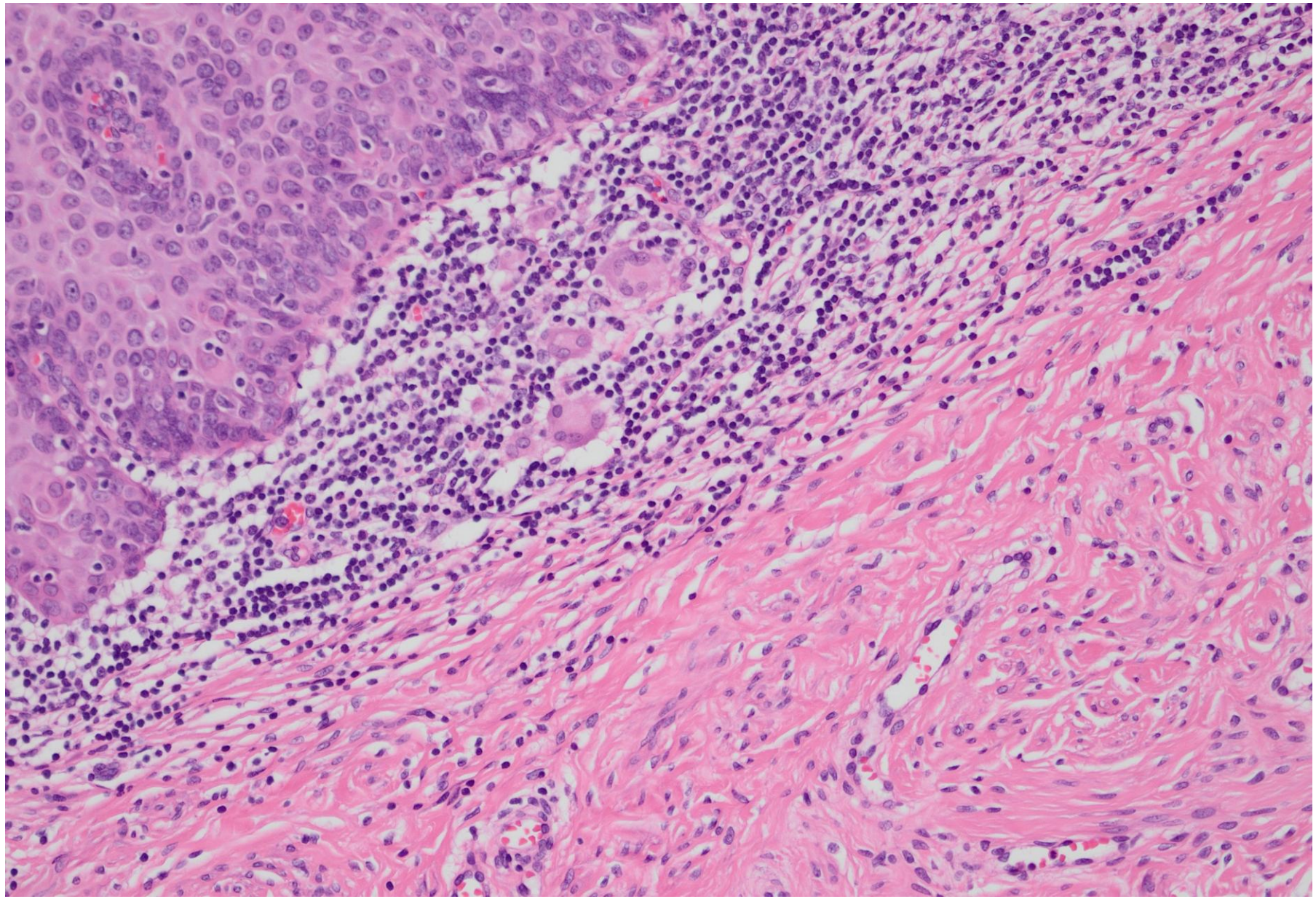
Cross- cutting artefact



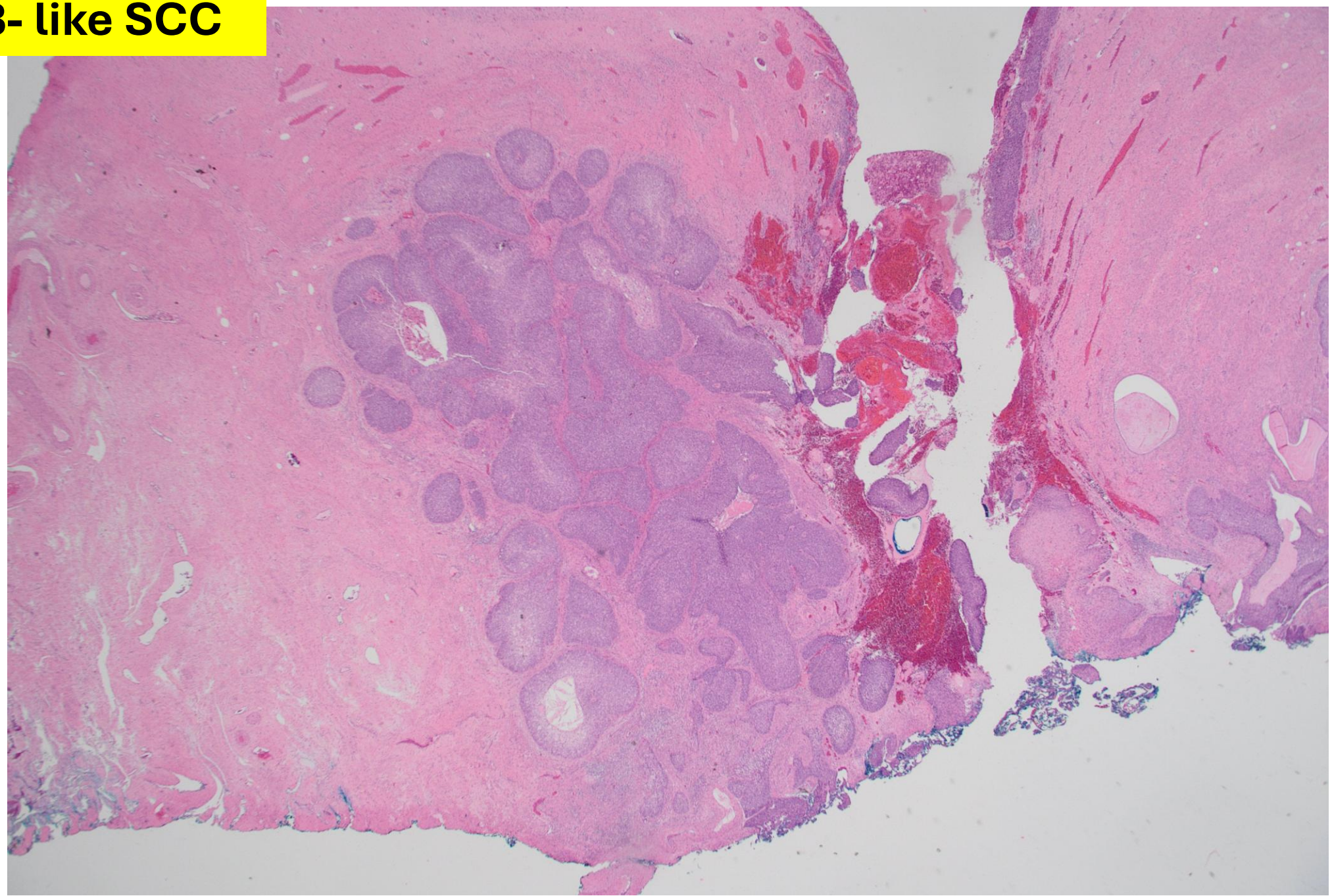
Biopsy artefact



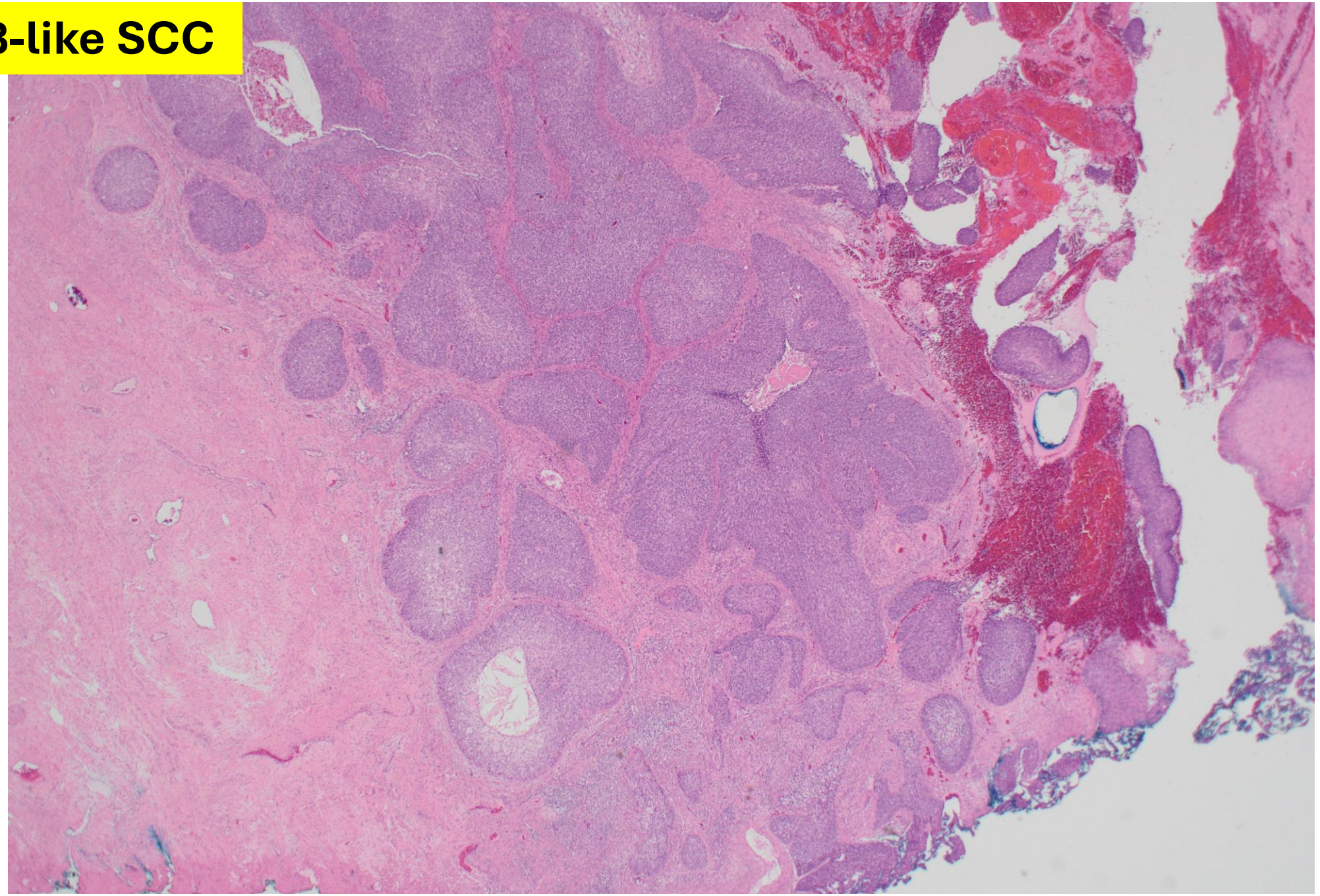




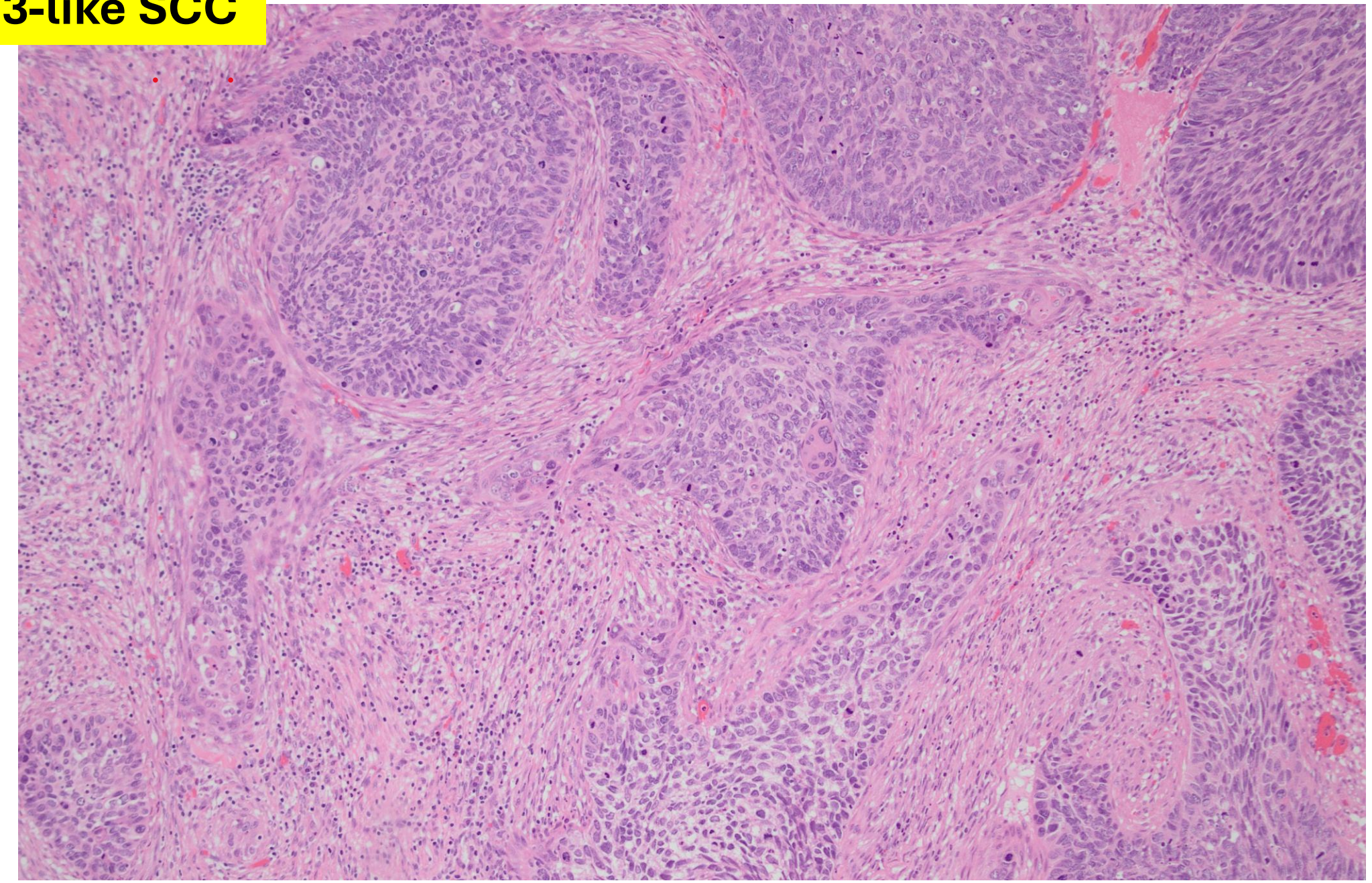
CIN3- like SCC



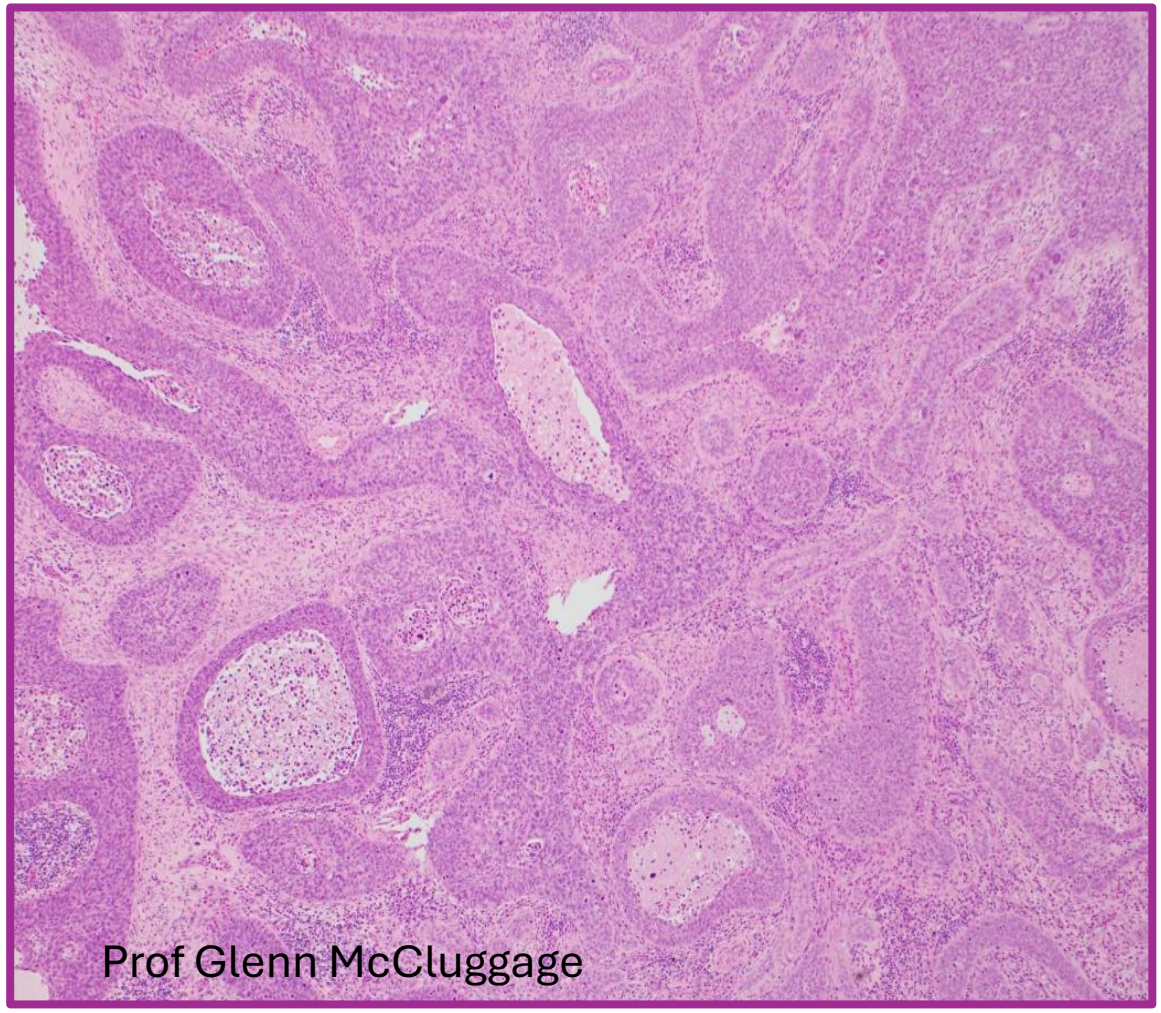
CIN3-like SCC



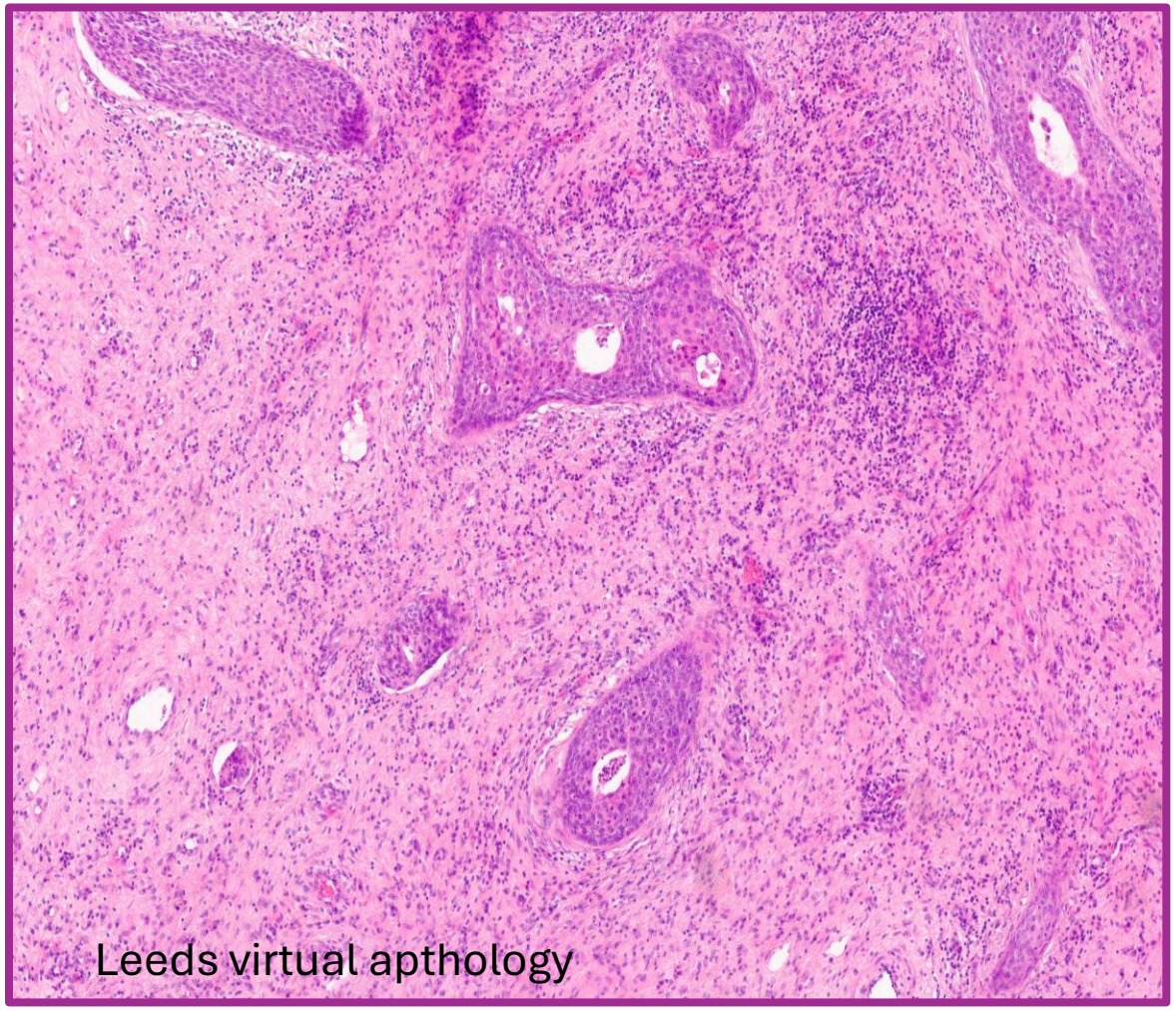
CIN3-like SCC



CIN3-like SCC

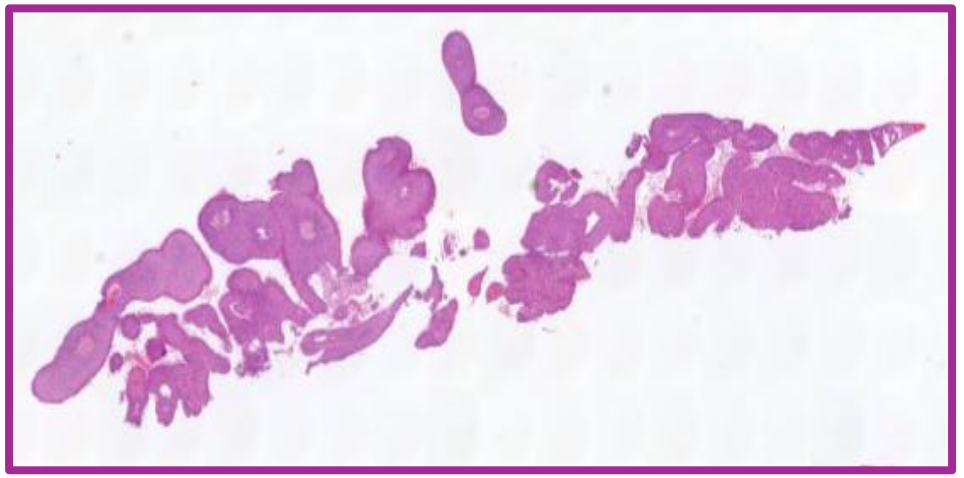


Prof Glenn McCluggage

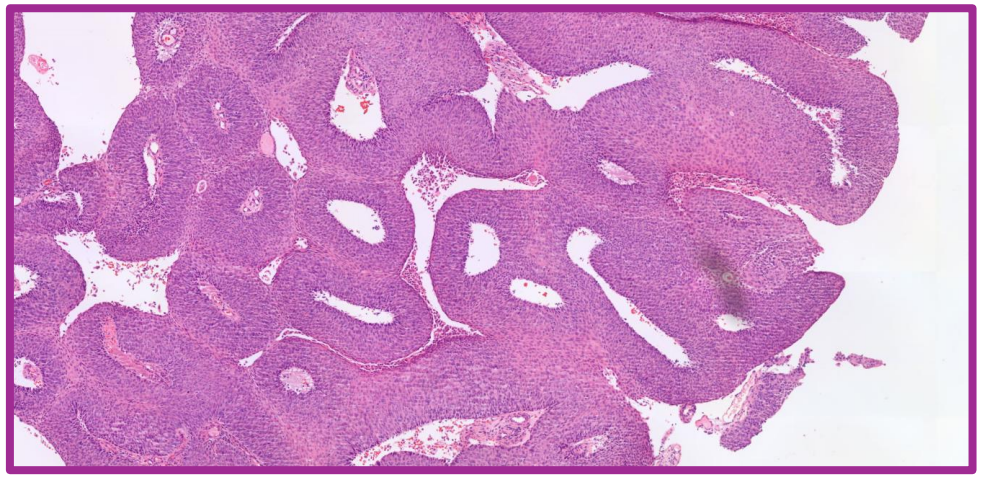


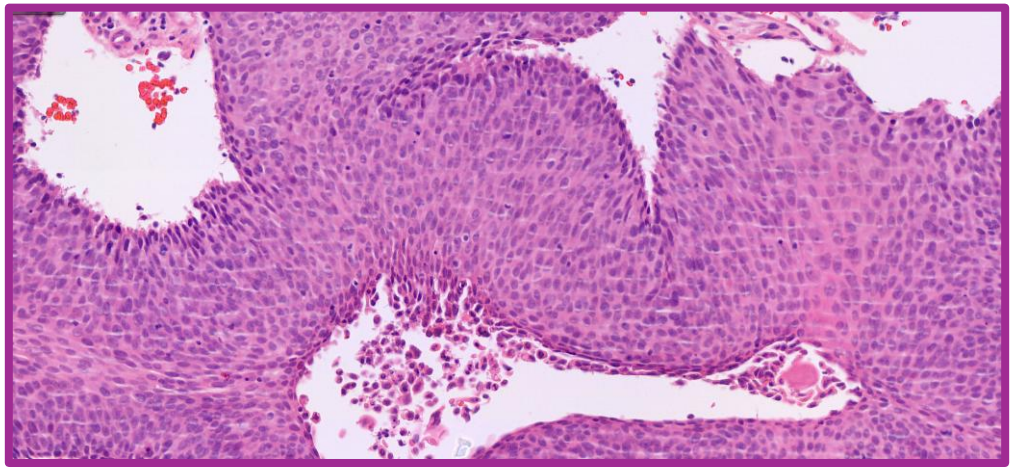
Leeds virtual apthology

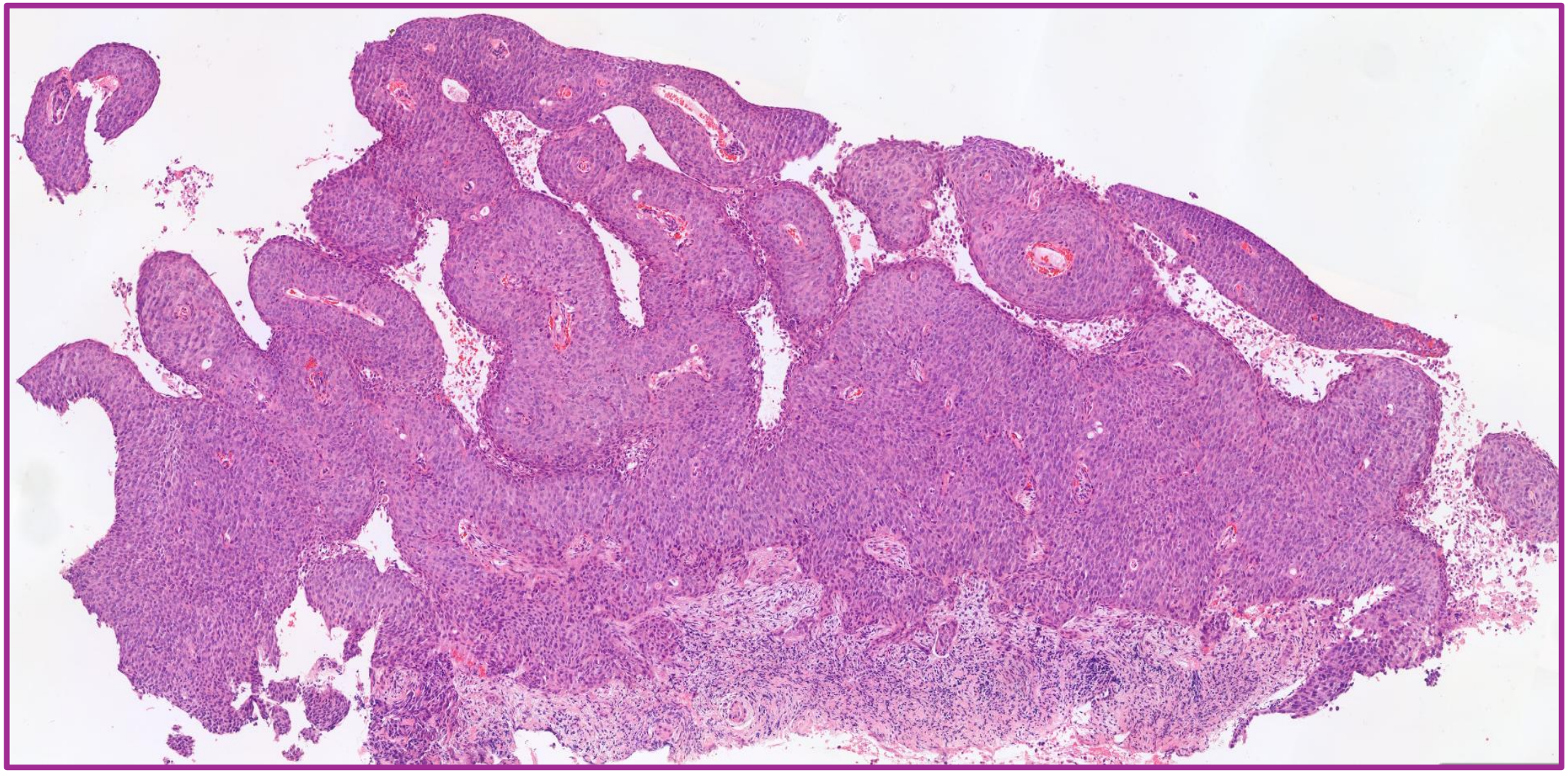
Papillary Squamous cell carcinoma



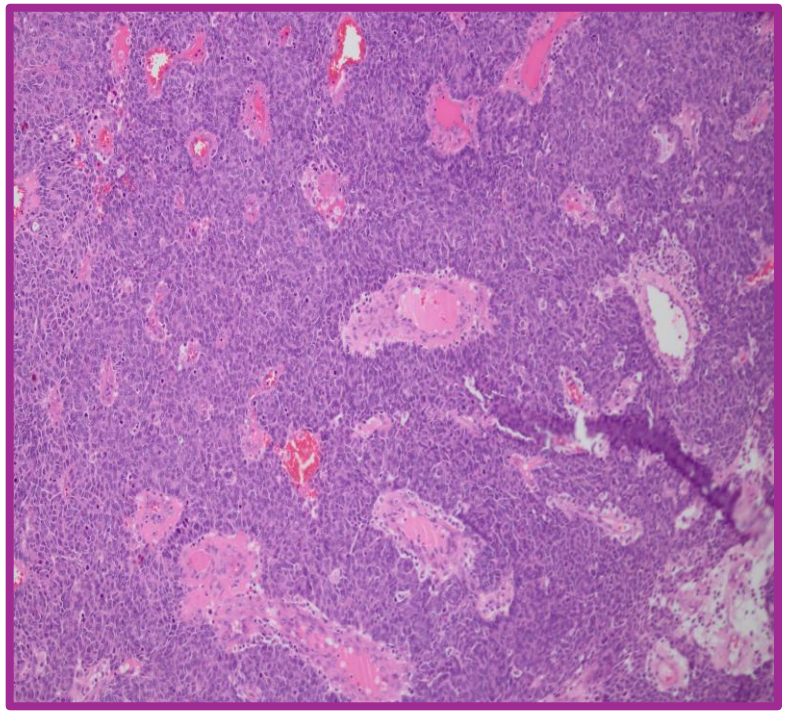
- Confluent papillary proliferation
- Fibrovascular cores
- Full thickness epithelial dysplasia
- Lack of koilocytosis/viral cytopathic effect

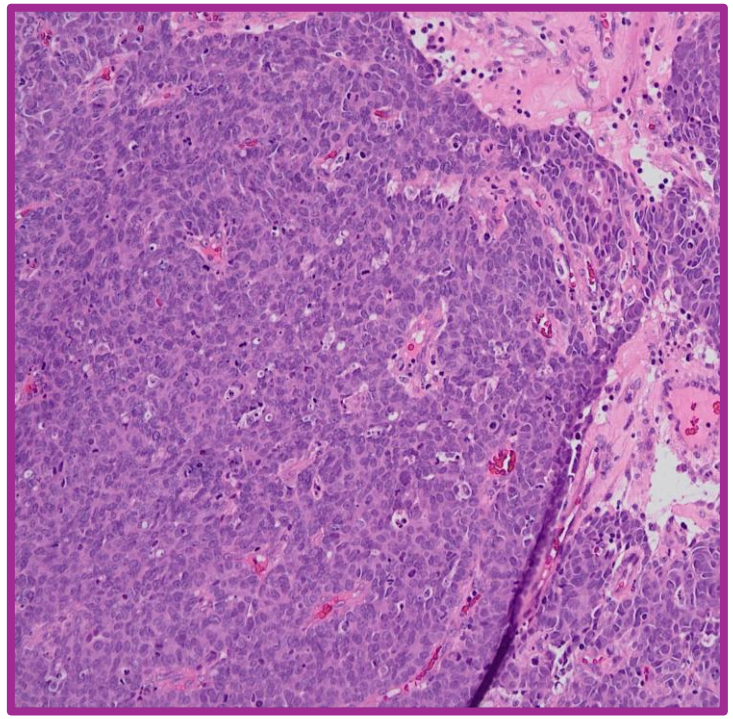


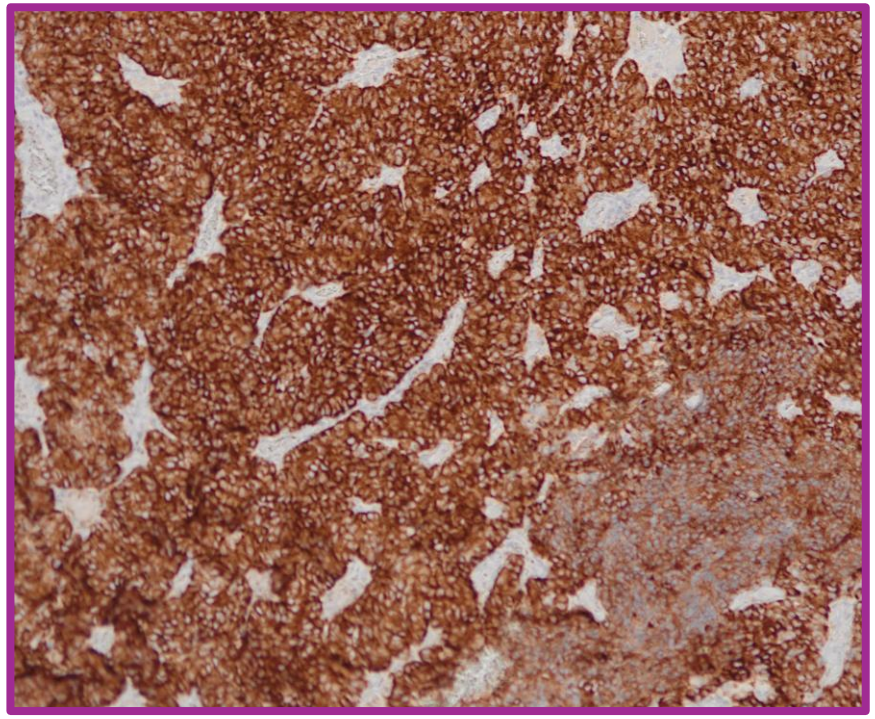




Neuroendocrine carcinoma



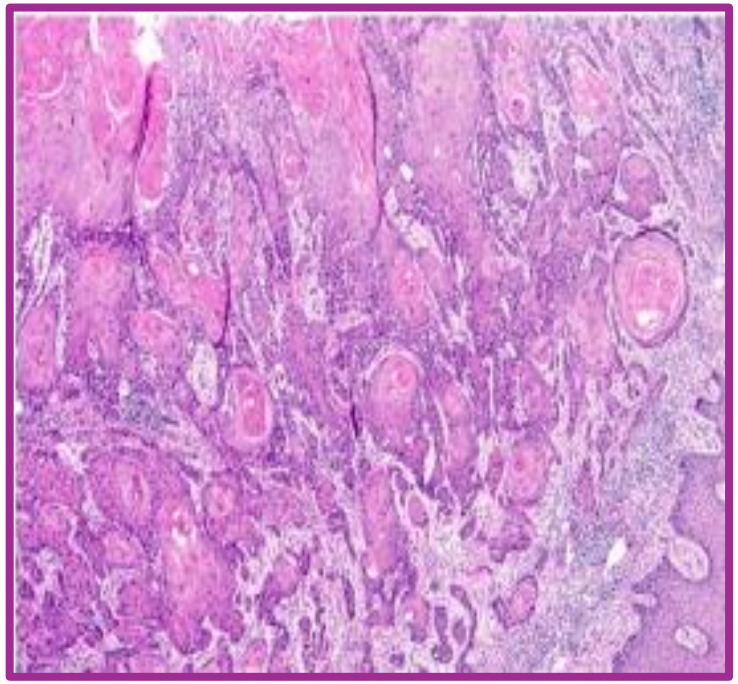
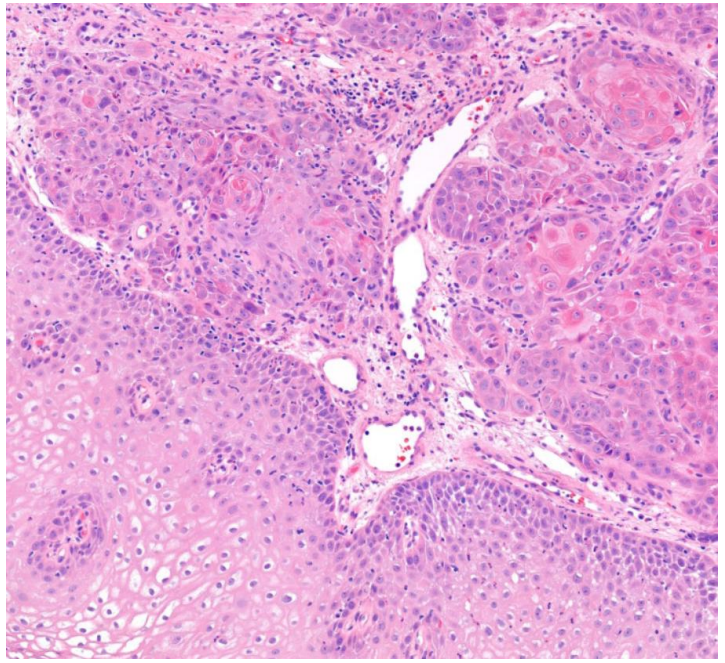
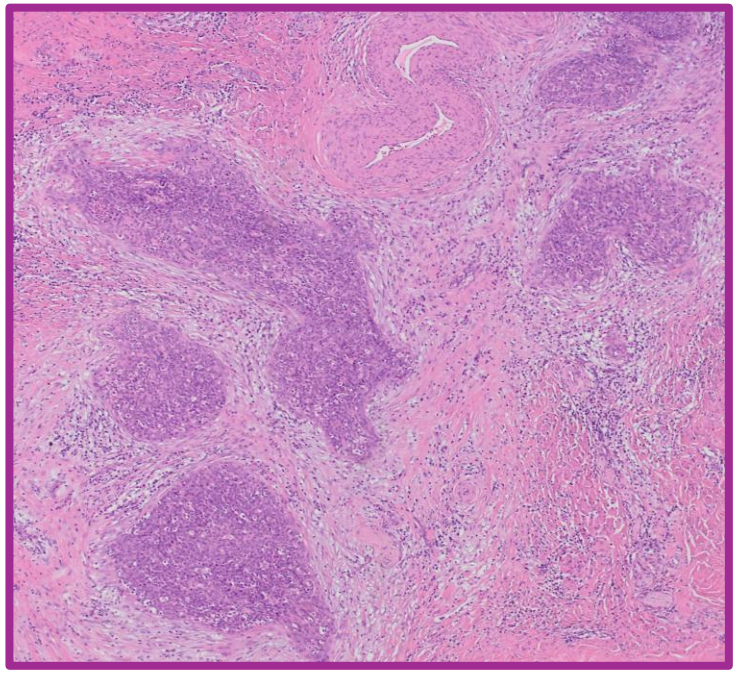




- NEC is a highly aggressive, variant with significantly worse prognosis
- Accurate diagnosis important to prevent undertreatment.

Broder's system

- Degree of keratinization, nuclear atypia, mitotic activity

- Almost all HPV-related cervical SCCs show a basaloid morphology and are thus poorly differentiated.
- Some studies have found that the keratinising variant of SCC has a poorer prognosis than the non-keratinising variant!
- Grading of very small superficially ('early') invasive carcinomas of is not possible or relevant.

Grading of SCC: ICCR guidance

- Not listed as a required but rather a recommended element in ICCR

- Not mandatory.
- You may still end up reporting it.
- Clinicians demand.

POLL 1

Which of the following pathology parameters does not influence clinical management?

A. Depth of invasion
B. LVSI
C. Tumour morphology (Keratinising, basaloid, papillary)
D. Margin status

POLL 1- Answer

- Which of the following pathology parameters does not influence clinical management of SCC?

A. Depth of invasion
B. LVSI
C. Keratinising vs basaloid subtypes
D. Margin status

Squamous Cell Carcinoma: Classification

- Keratinising
- Nonkeratinising
- Basaloid
- Warty
- Verrucous
- Squamotransitional/Papillary
- Lymphoepithelioma-like

WHO 2014 → WHO 2020

- SCC-HPV Associated
- SCC-HPV Independent

HPV based classification - Rationale

- Aligns classification across lower genital tract sites
- Prognostically relevant
- Helps to estimate the impact of screening programme
- Helps to assess the effectiveness of HPV vaccination
- Will assist the development of future screening strategies

HPV based classification

HPV-A vs HPV-I tumors:

- Significant morphologic overlap
- Cannot be reliably distinguished based on morphology alone

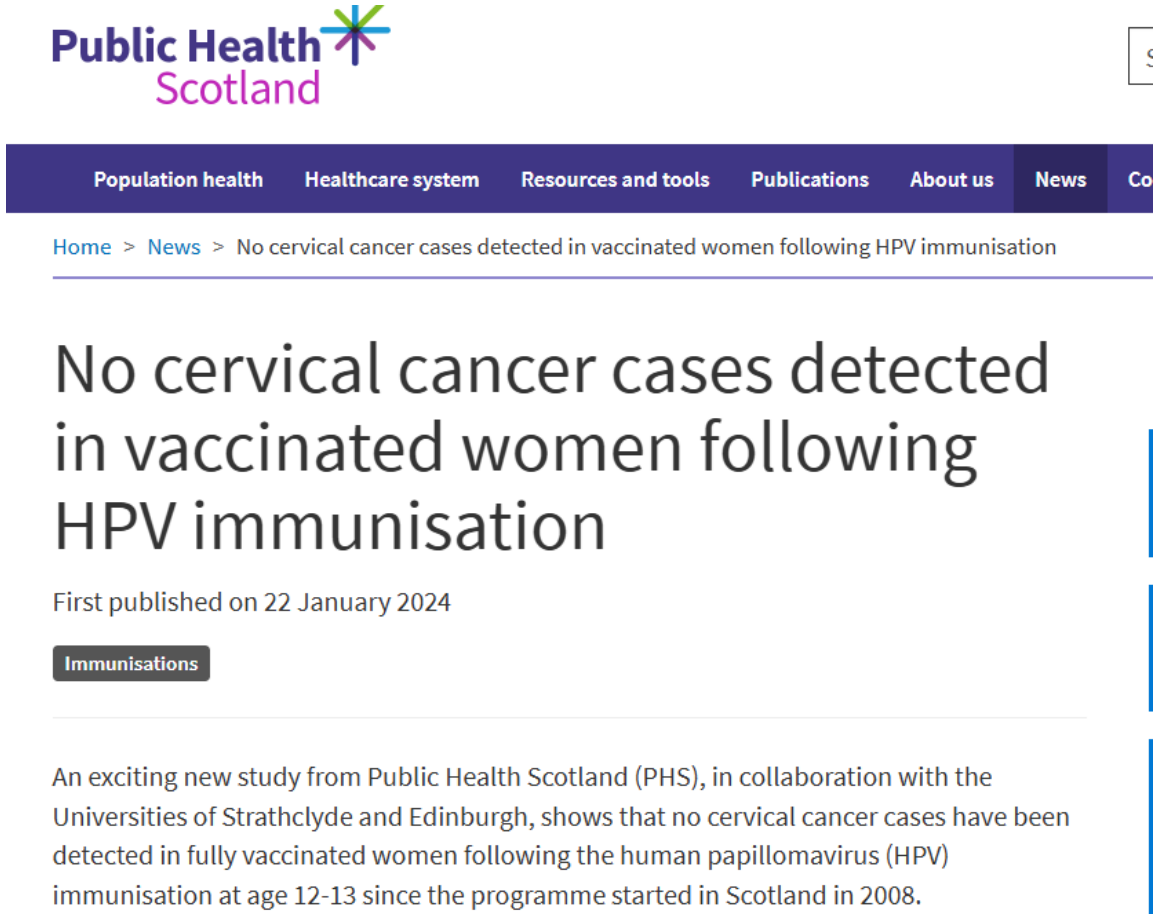
Ancillary tests –
WHICH and WHEN?

Ancillary tests

- P16 is an excellent surrogate marker for HR HPV
  - Should we be doing p16 in all the cases of SCC?
- If p16 negative – consider further tests
  - HPV FISH/PCR
- If none accessible
  - Presence of typical HSIL/CIN3 and/or
  - HR HPV in referral smear sufficient to categorise the process as HPV-A.
- **SCC NOS**

HPA-associated SCC

- >95% of cervical SCC are HPV-A tumours.
- Proportion expected to decline with the success of the HPV vaccination programme



HPV independent SCC

Modern Pathology
Volume 38, Issue 6, June 2025, 100742

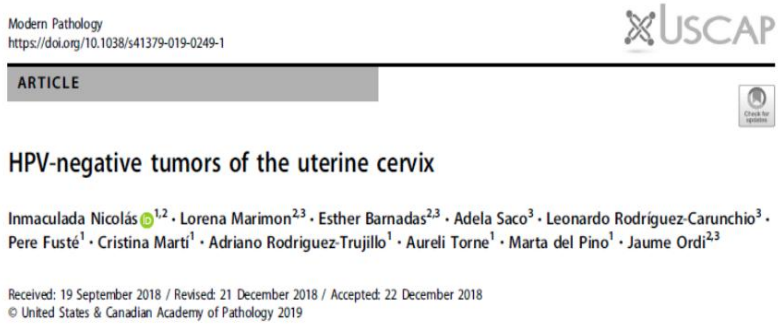
Research Article

Cervical Human Papillomavirus–Independent Squamous Cell Carcinoma: A Clinicopathological Review and Outcomes Analysis Compared With Human Papillomavirus–Associated Squamous Cell Carcinoma

Simona Stolnicu [a], Natalia Rakislova [b c d], Alba Morató [b d], Douglas Allison [e], Nuria Carreras Dieguez [b], Lien Hoang [f], Andrei Patrichi [a], Antonio Ieni [g], Ana Felix [h], Anna Pesci [i], Claudia Mateoiu [j], Esther Guerra [k], Rouba Ali-Fehmi [l m], Mira Kheil [l m], Andres Roma [n], Oluwole Fadare [n], Gulisa Turashvili [o p], Esther Oliva [p], Kyle M. Devins [p], Carlos Parra-Herran [q]...
Robert A. Soslow [x]

Am J Surg Pathol. 2023 Dec 1;47(12):1376-1389. doi: 10.1097/PAS.0000000000002122. Epub 2023 Sep 13.

Incidence and Clinicopathologic Characteristics of Human Papillomavirus–independent Invasive Squamous Cell Carcinomas of the Cervix: A Morphologic, Immunohistochemical, and Human Papilloma–Virologic Study of 670 Cases



Modern Pathology
https://doi.org/10.1038/s41379-019-0249-1

ARTICLE

HPV-negative tumors of the uterine cervix

Inmaculada Nicolás [1,2] · Lorena Marimon [2,3] · Esther Barnadas [2,3] · Adela Saco [3] · Leonardo Rodríguez-Carunchio [3] · Pere Fusté [1] · Cristina Martí [1] · Adriano Rodríguez-Trujillo [1] · Aureli Torne [1] · Marta del Pino [1] · Jaume Ordi [2,3]

Received: 19 September 2018 / Revised: 21 December 2018 / Accepted: 22 December 2018

HPV independent SCC

- More common in older women (Mean age 68 years)
- Advanced tumour stage at presentation
- Keratinising morphology more common
- Both p53 mutant and p53 wild type described
- Poor prognosis compared to HPV-A tumours

- Morphology not helpful in detecting HPV status
- Ancillary tests (p16, HPV ISH, p53) required
- (especially in patient >60 years)

HPV- independent SCC - Precursor lesions

- Differentiated and keratinizing lesions common (like differentiated vulvar intraepithelial neoplasia- dVIN)
- Basaloid morphology and lesions resembling VaVIN (verruciform, acanthotic, p53 wild-type, HPV-negative) also reported

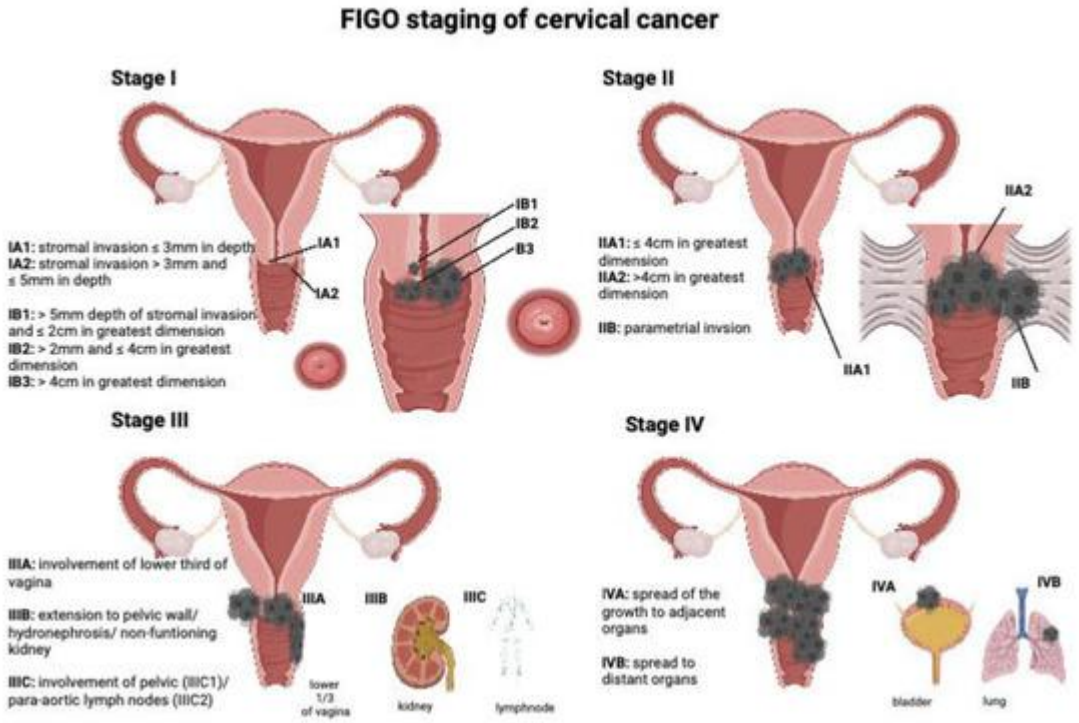
- Terminology proposed: dCIN (differentiated CIN) and VaCIN

- Limited data .....More studies required .....

False negative HPV test

- Assay failure
- Poor fixation /suboptimal sample
- Limited HPV subtype coverage
- Low viral load below PCR detection thresholds
- Latent HPV infection

FIGO staging 2018



Stage	Description
I	Carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only with microscopy, with maximum depth of invasion <5 mm
IA1	Stromal invasion <3 mm in depth
IA2	Stromal invasion ≥3 mm and <5 mm in depth
IB	Invasive carcinoma confined to the uterine cervix, with measured deepest invasion ≥5 mm
IB1*	Tumor measures <2 cm in greatest dimension
IB2*	Tumor measures ≥2 cm and <4 cm in greatest dimension
IB3*	Tumor measures ≥4 cm in greatest dimension
II	Carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall
IIA	Limited to the upper two-thirds of the vagina without parametrial involvement
IIA1	Tumor measures <4 cm in greatest dimension
IIA2	Tumor measures ≥4 cm in greatest dimension
IIB	With parametrial involvement but not up to the pelvic wall
III	Carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes
IIIA	Involves the lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney from tumor
IIIC*	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent†
IIIC1*	Pelvic lymph node metastasis only
IIIC2*	Para-aortic lymph node metastasis
IV	Carcinoma has extended beyond the true pelvis or has involved (biopsy-proven) the mucosa of the bladder or rectum
IVA	Spread to adjacent pelvic organs
IVB	Spread to distant organs

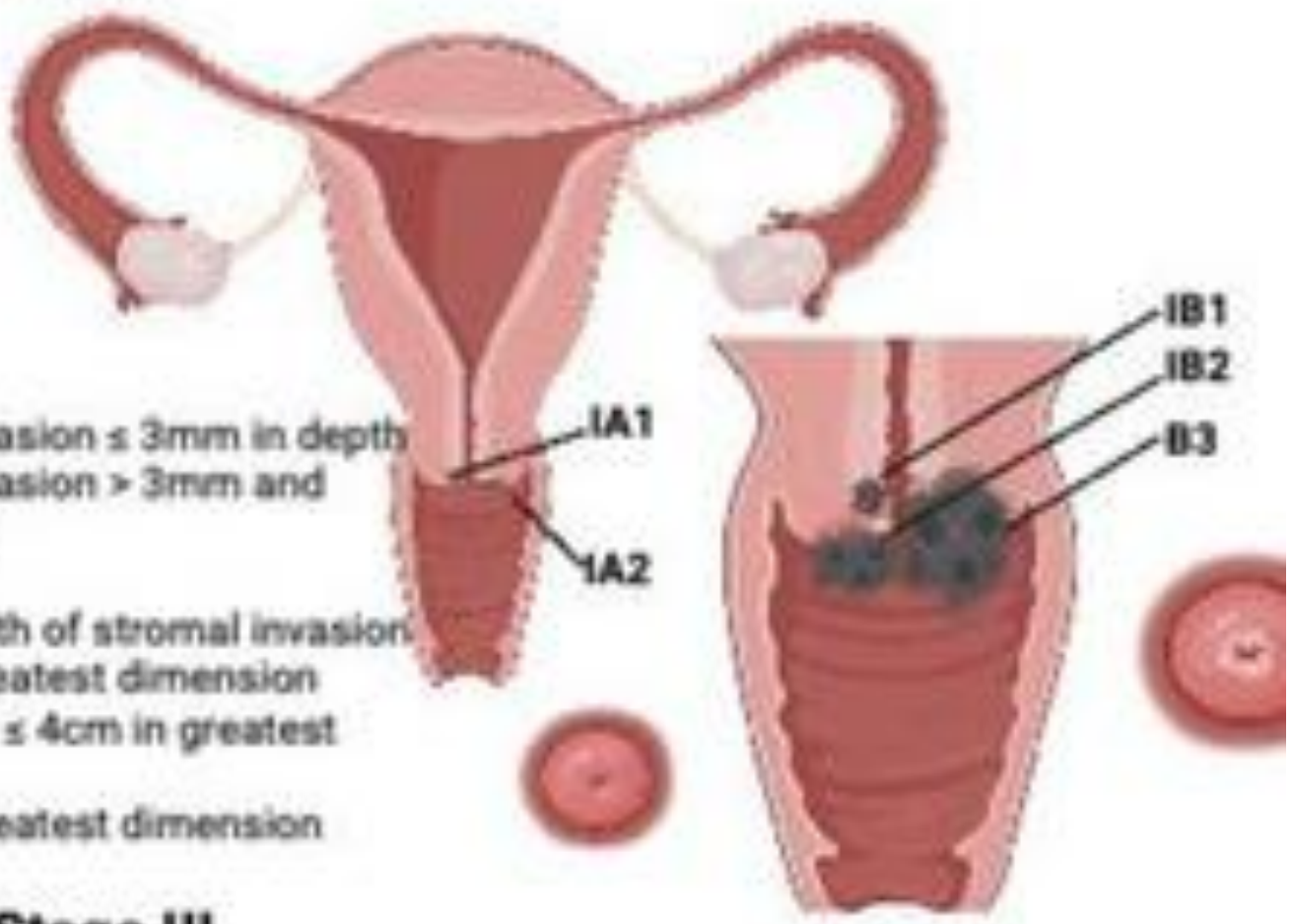
Note.— Imaging and pathologic analysis, where available, can be used to supplement clinical findings for all stages. FIGO = International Federation of Gynecology and Obstetrics. (Adapted, under a CC BY license, from reference 1.)

* Indicates stages that are new from the 2009 FIGO system.

† Stage IIIC should be annotated with *r* (radiology) or *p* (pathologic analysis) to indicate the method used to allocate this stage. Imaging modality or pathologic technique should also be documented.

Medicina**2023**, *59*(5), 925

Stage I



IA1: stromal invasion ≤ 3mm in depth
IA2: stromal invasion > 3mm and ≤ 5mm in depth

IB1: > 5mm depth of stromal invasion and ≤ 2cm in greatest dimension
IB2: > 2mm and ≤ 4cm in greatest dimension
IB3: > 4cm in greatest dimension

Stage III

FIGO 2018

IA Invasive carcinoma that can be diagnosed only by microscopy with maximum depth of invasion ≤5 mm

- 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) **confined to cervix**

- 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

Accurate measurement is critical

- **IA1**
  - Cone biopsy/LLETZ (if margins clear) or simple hysterectomy
- **IA2**:
  - Cone biopsy/LLETZ with lymph node assessment or
  - Trachelectomy /radical hysterectomy with lymphadenectomy
- **IB1 (≤2 cm)**:
  - Radical hysterectomy + pelvic lymphadenectomy
  - Radical trachelectomy with lymph node assessment
- **IB2 (>2 cm and ≤4 cm)** and **IB3 (>4 cm)**:
  - Radical hysterectomy + lymphadenectomy or
  - Primary chemoradiation

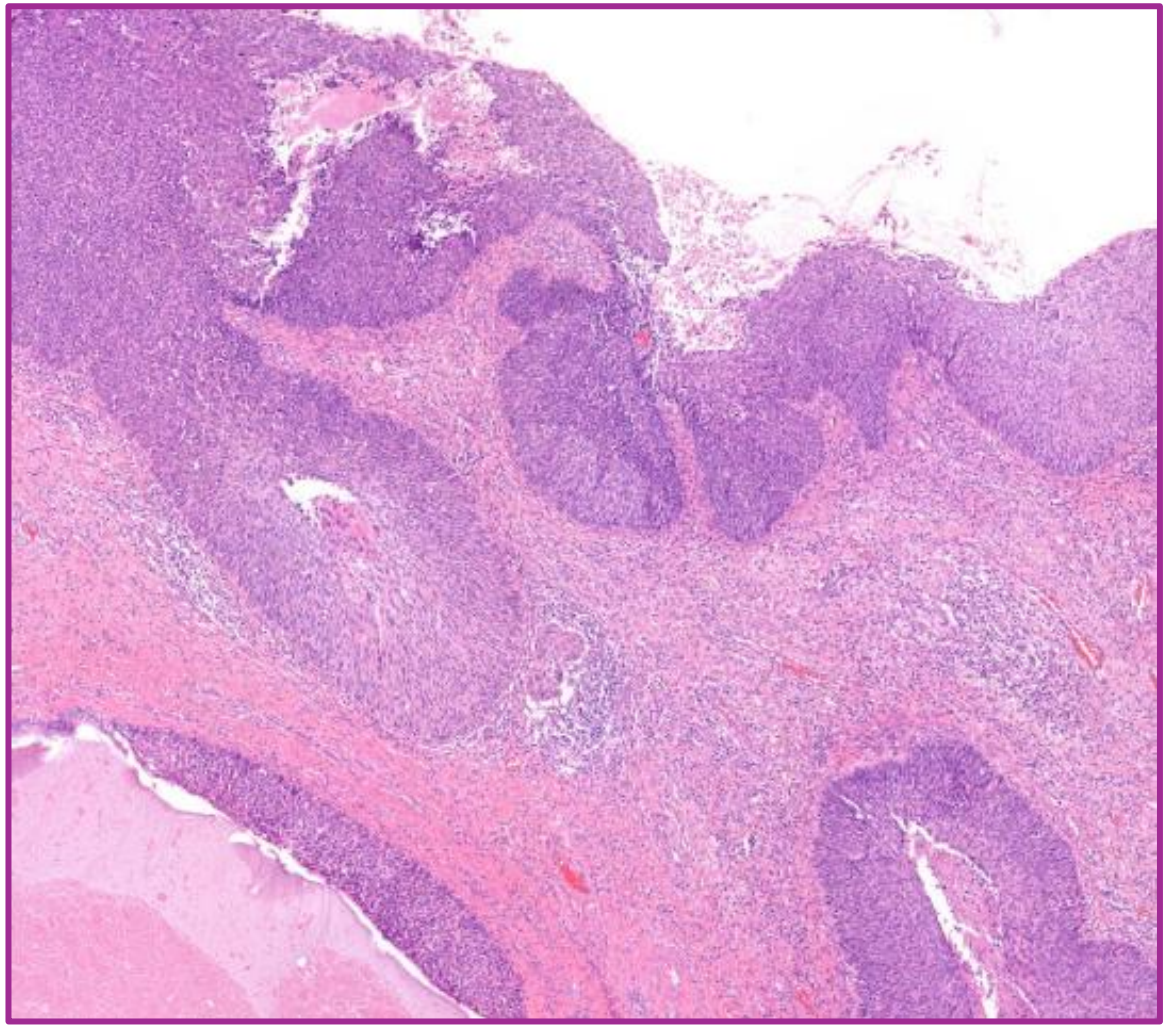
- Lymph node status **guides adjuvant therapy**
- Fertility-sparing options **considered only in select early-stage cases**

- **Accurate staging requires**

Correct estimation of DOI

Correct estimation of the tumour size.

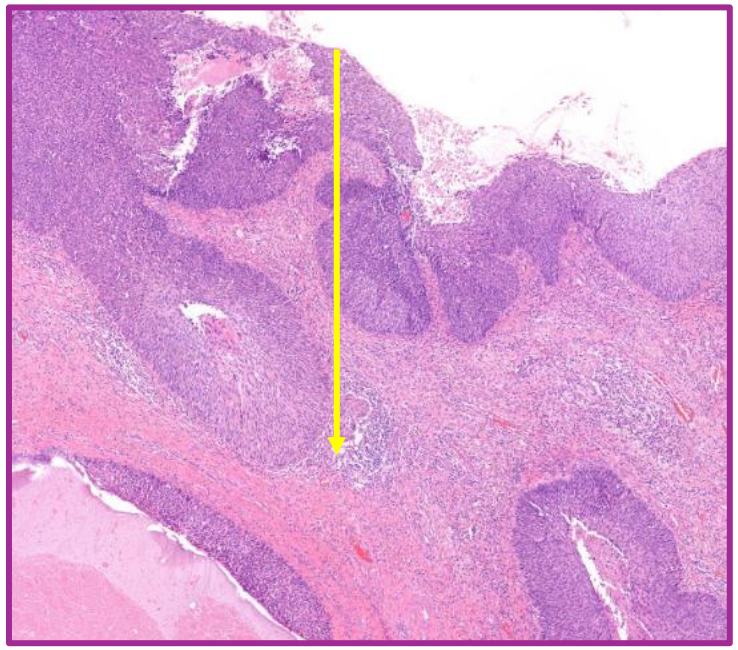
Poll 2



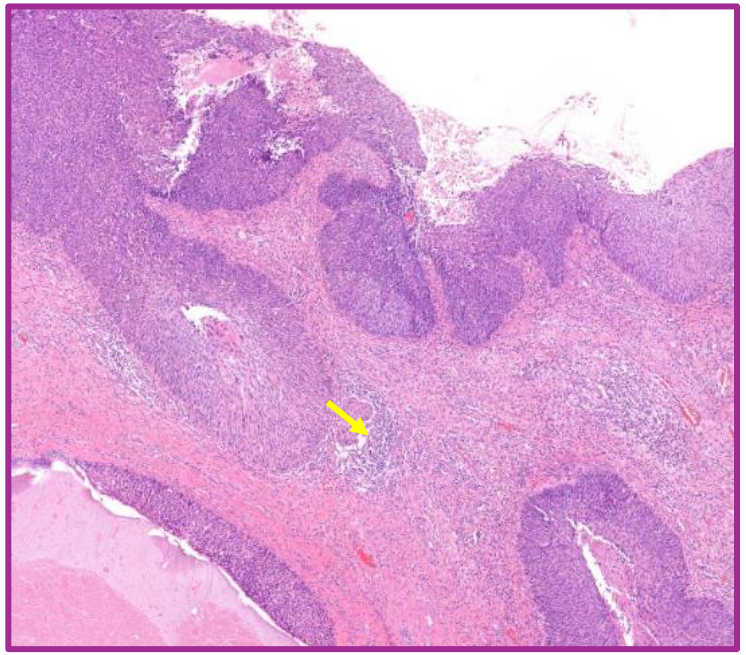
POLL 2- Which one is correct?

Which one of the following' depth of invasion' measurement is correct?

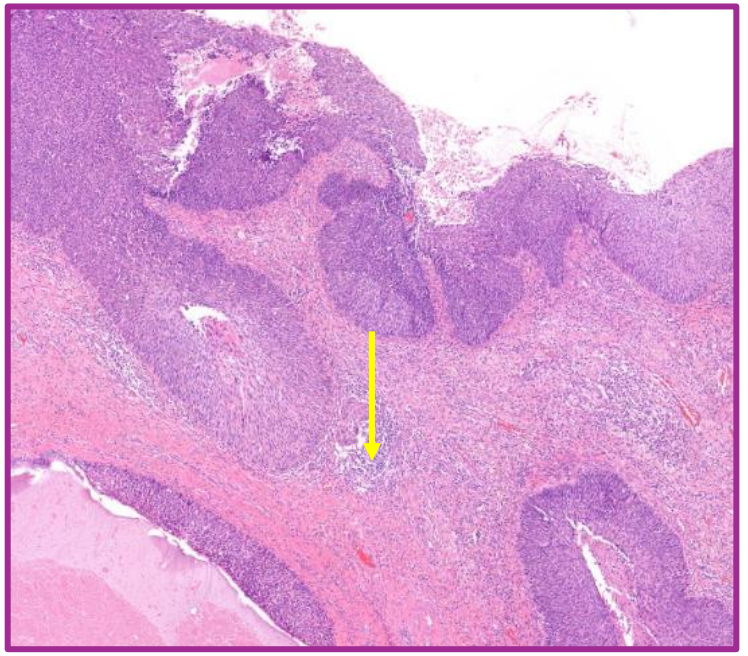
A



B



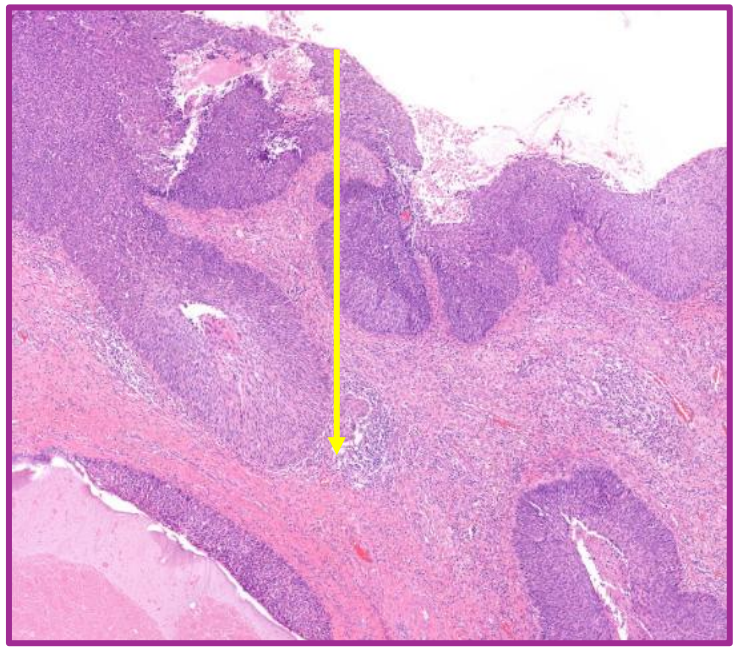
C



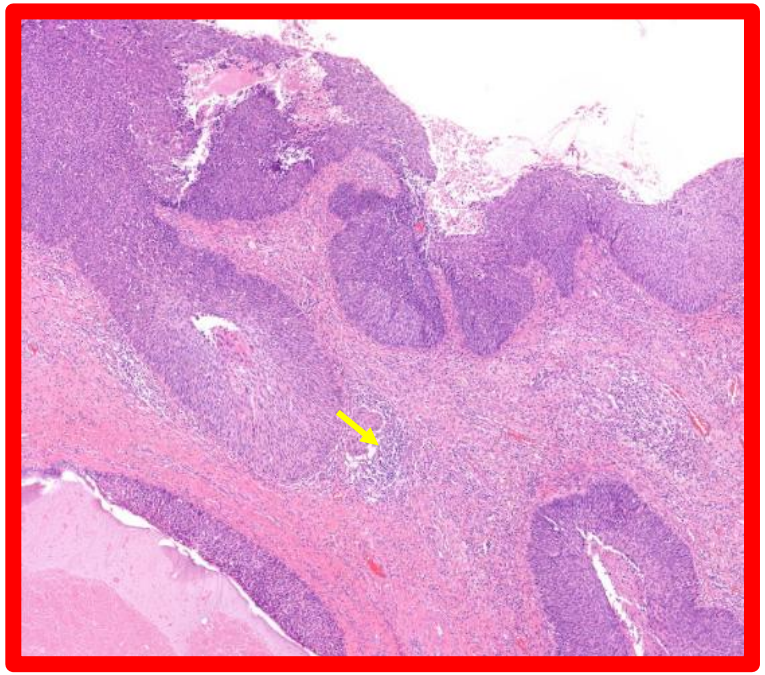
POLL 2- Answer

Which one of the following' depth of invasion' measurement is correct?

A



B



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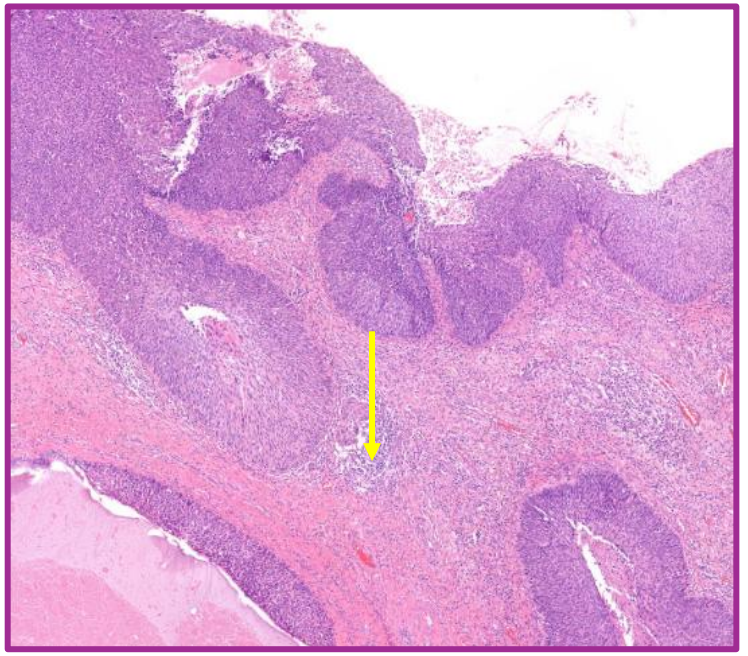
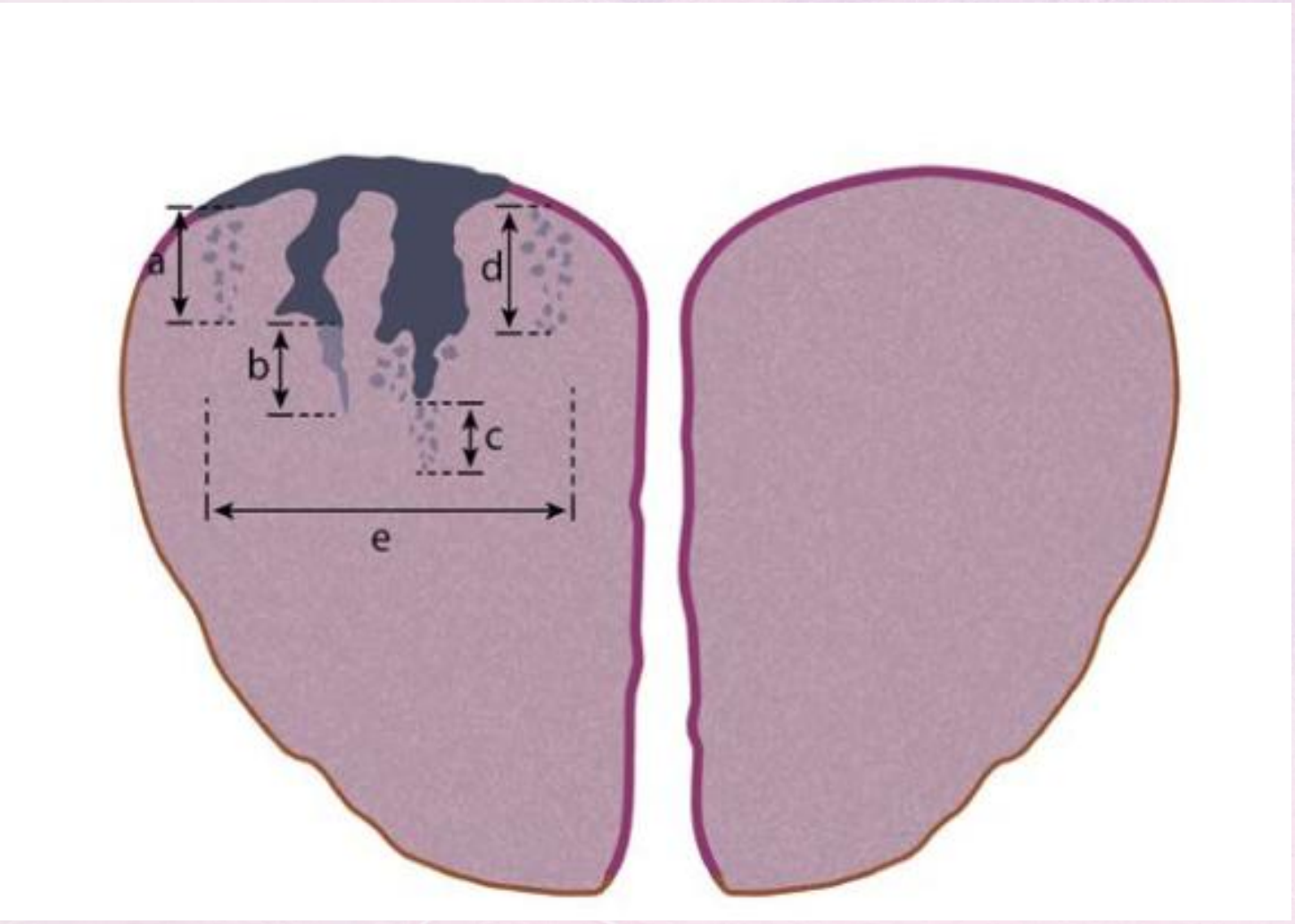


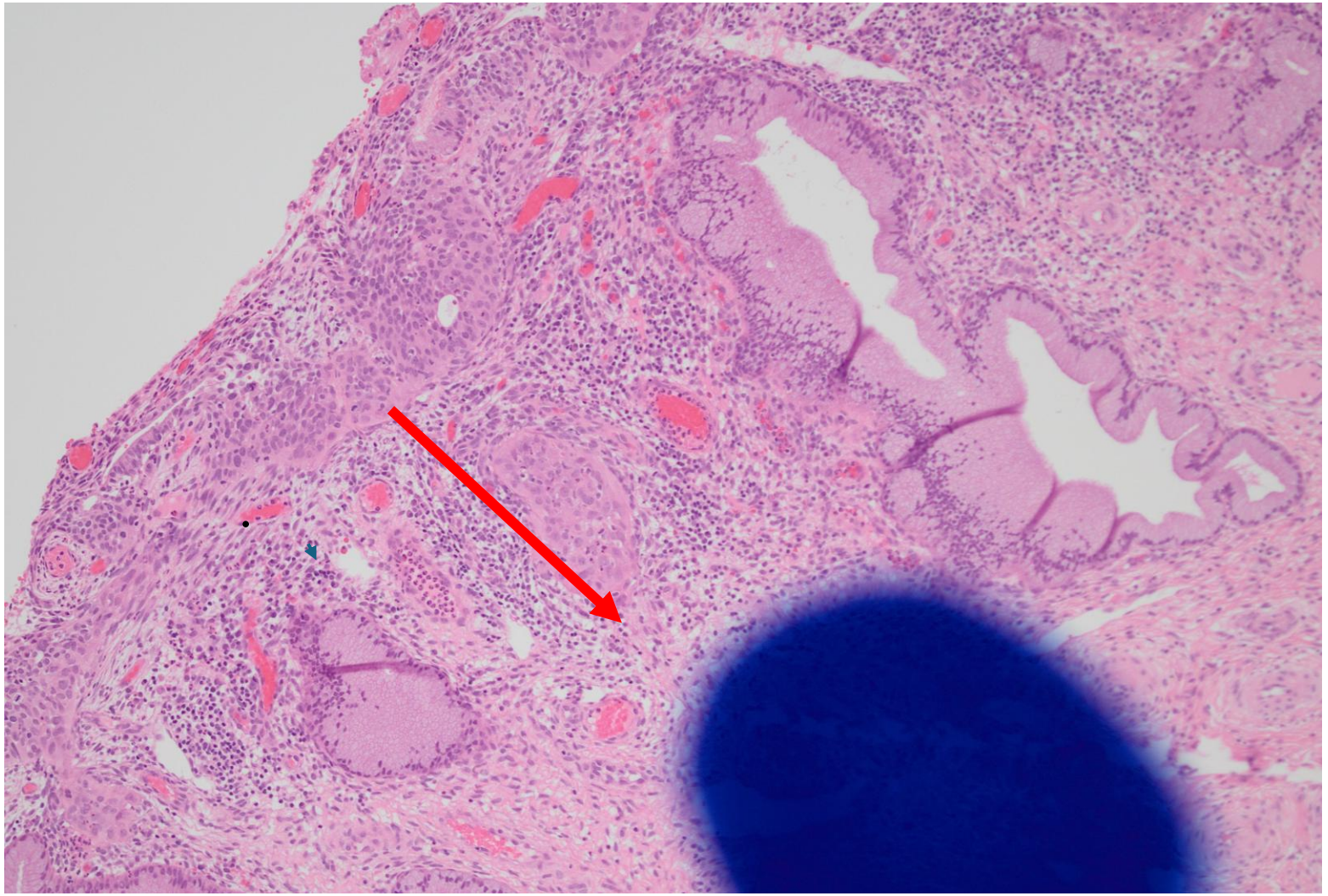
Tumour measurement –

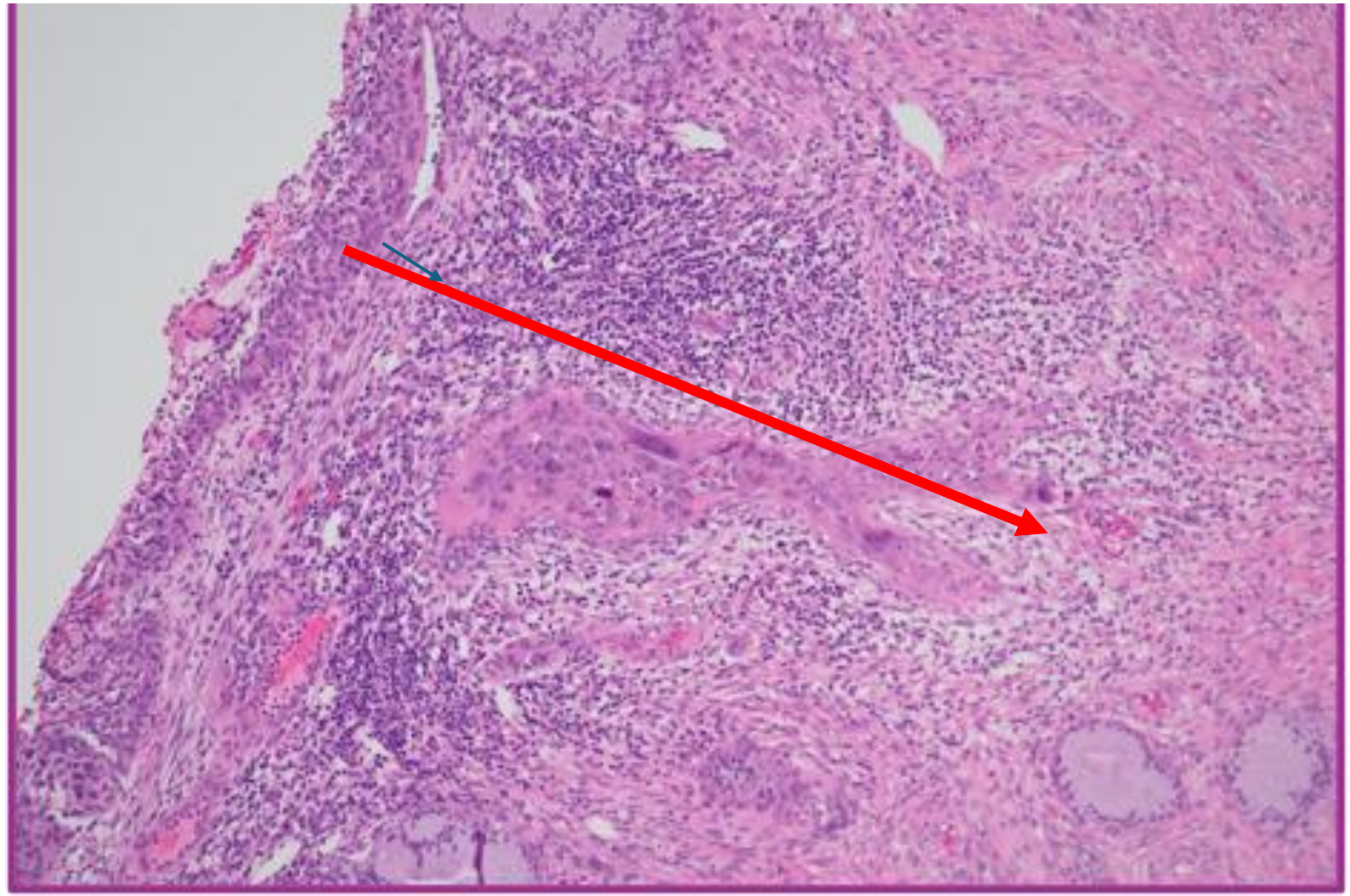
- Measuring DOI
- Exophytic tumours
- Ulcerated tumours
- Multifocal tumours
- Multiple specimens

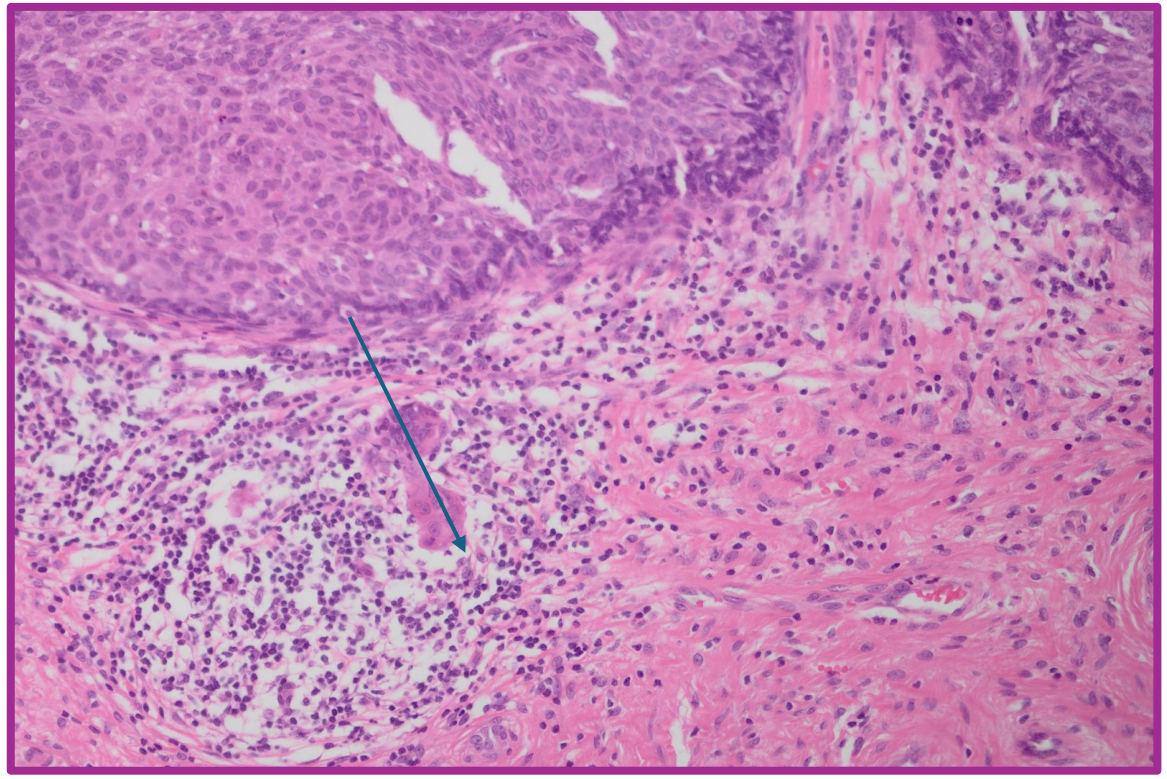
Accurate measurement critical for patient management.

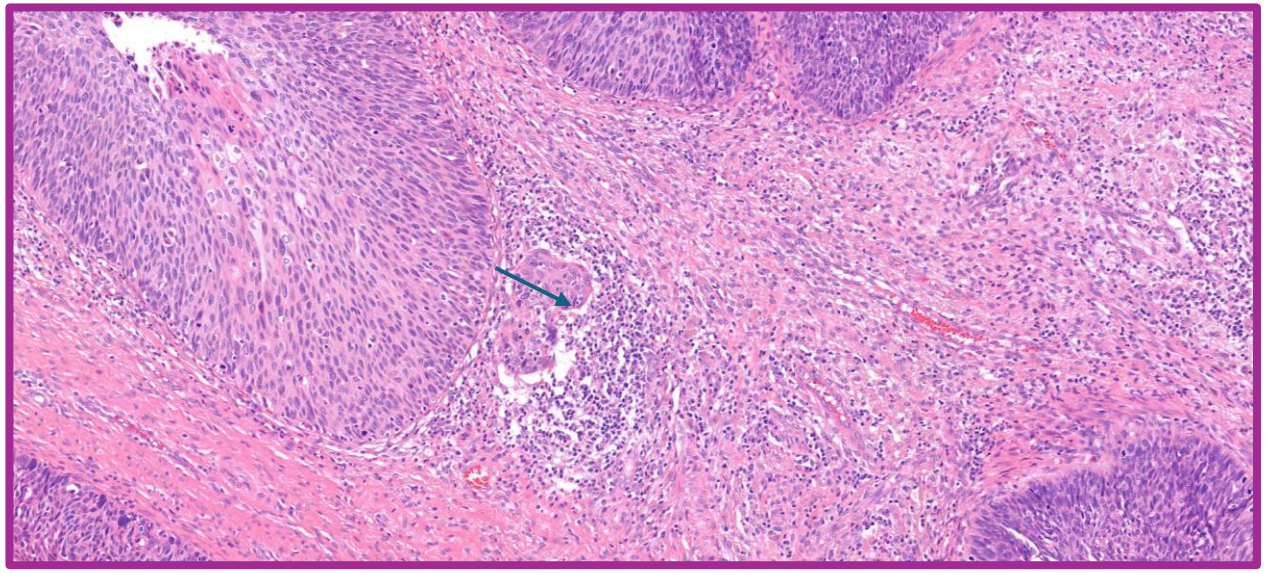


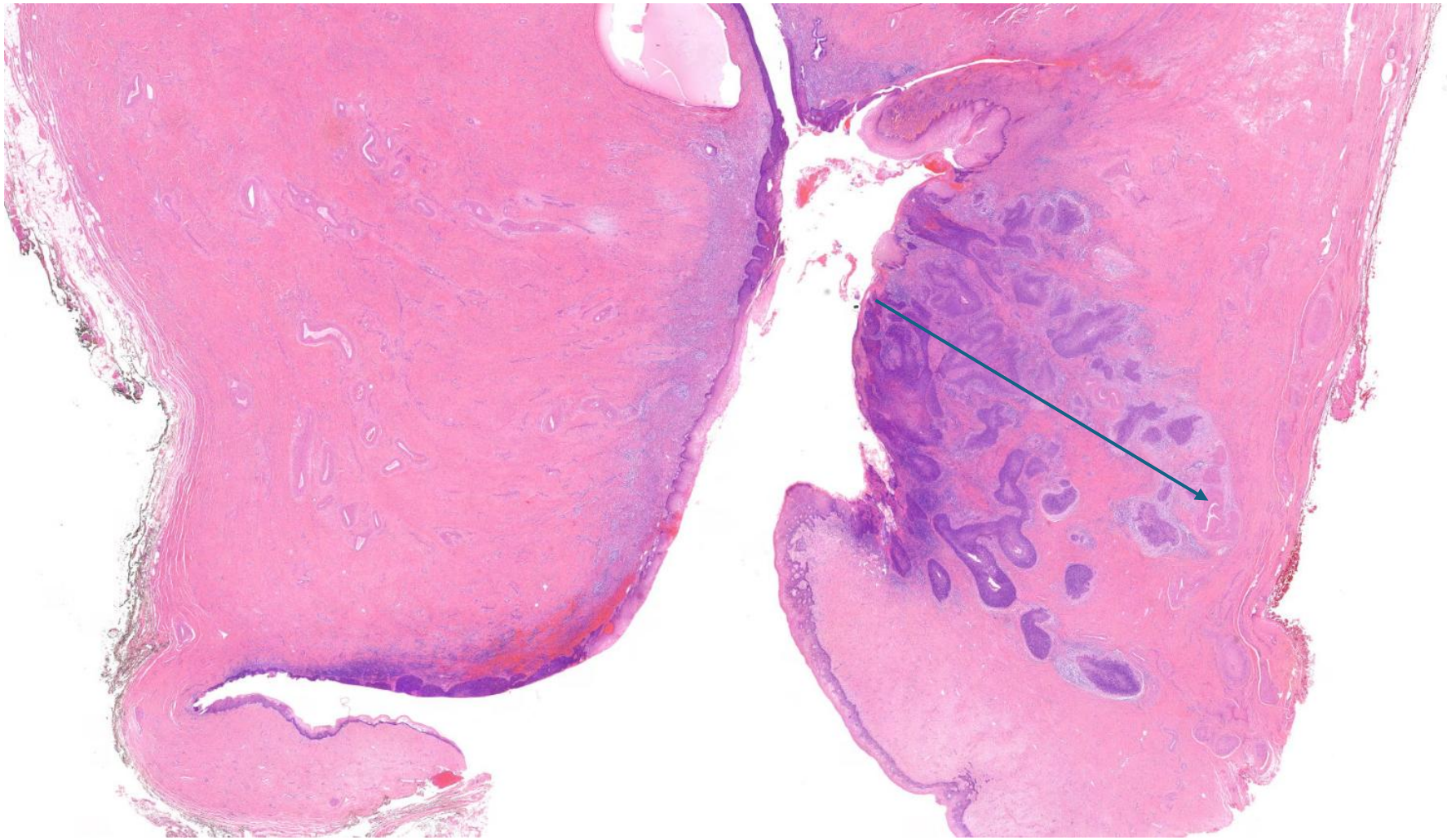
- From base of the surface epithelial stromal junction to the deepest focus
- If denuded – from the surface to the deepest focus
- From base of the crypt from where the invasive focus is arising to the deepest focus of invasion
- If the deepest point of invasion involves the deep margin of the specimen, comment should be made regarding the possibility of underestimation



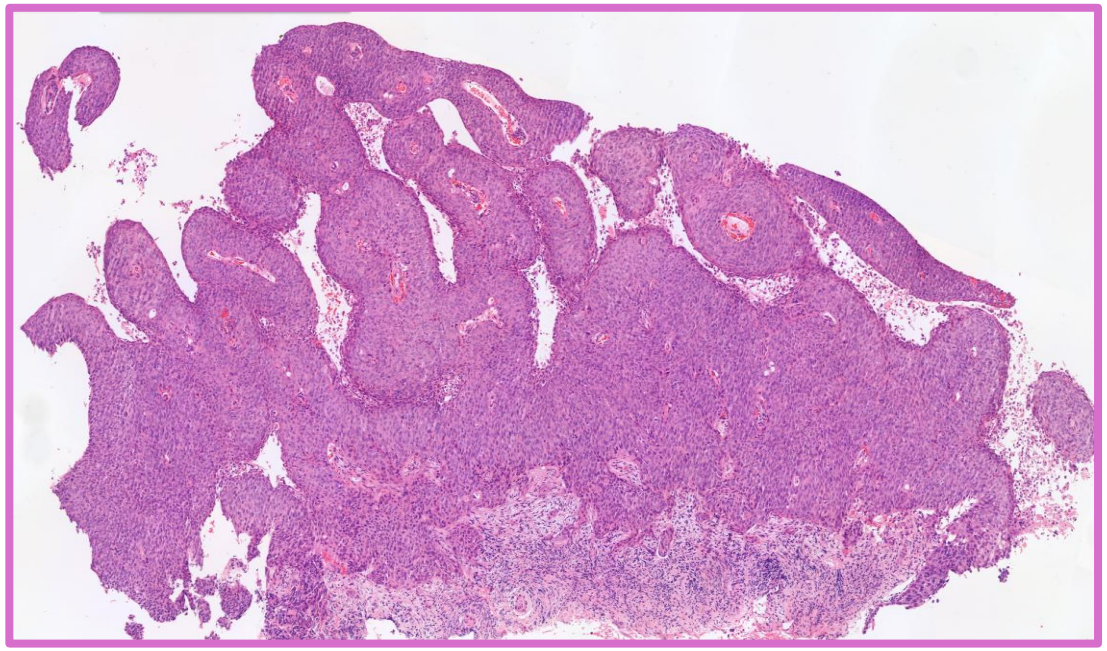


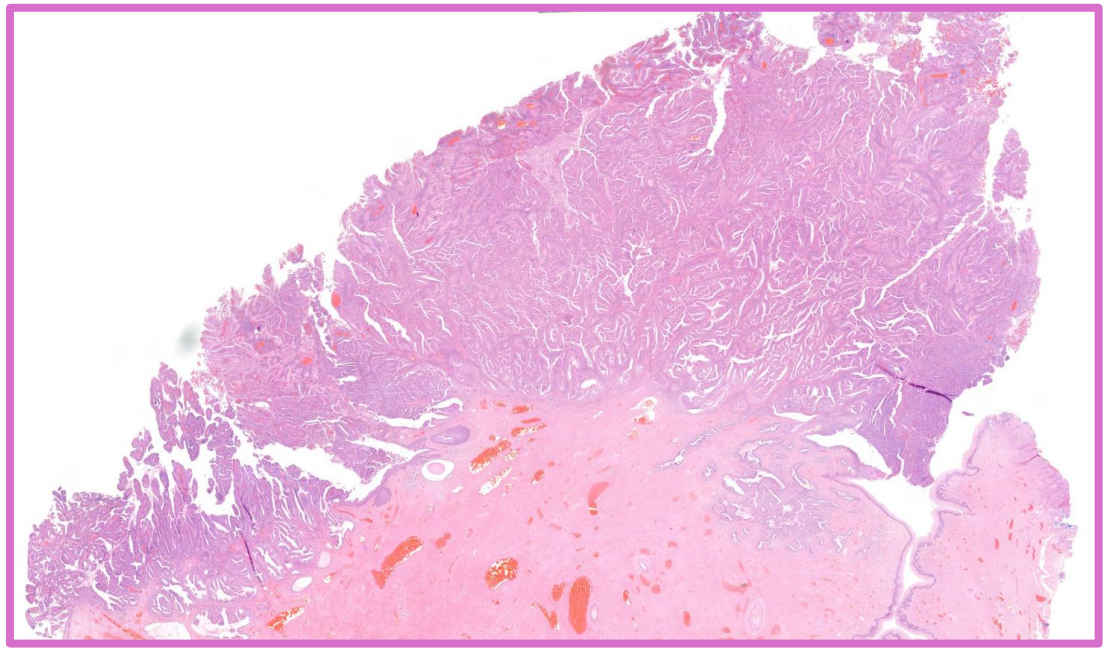




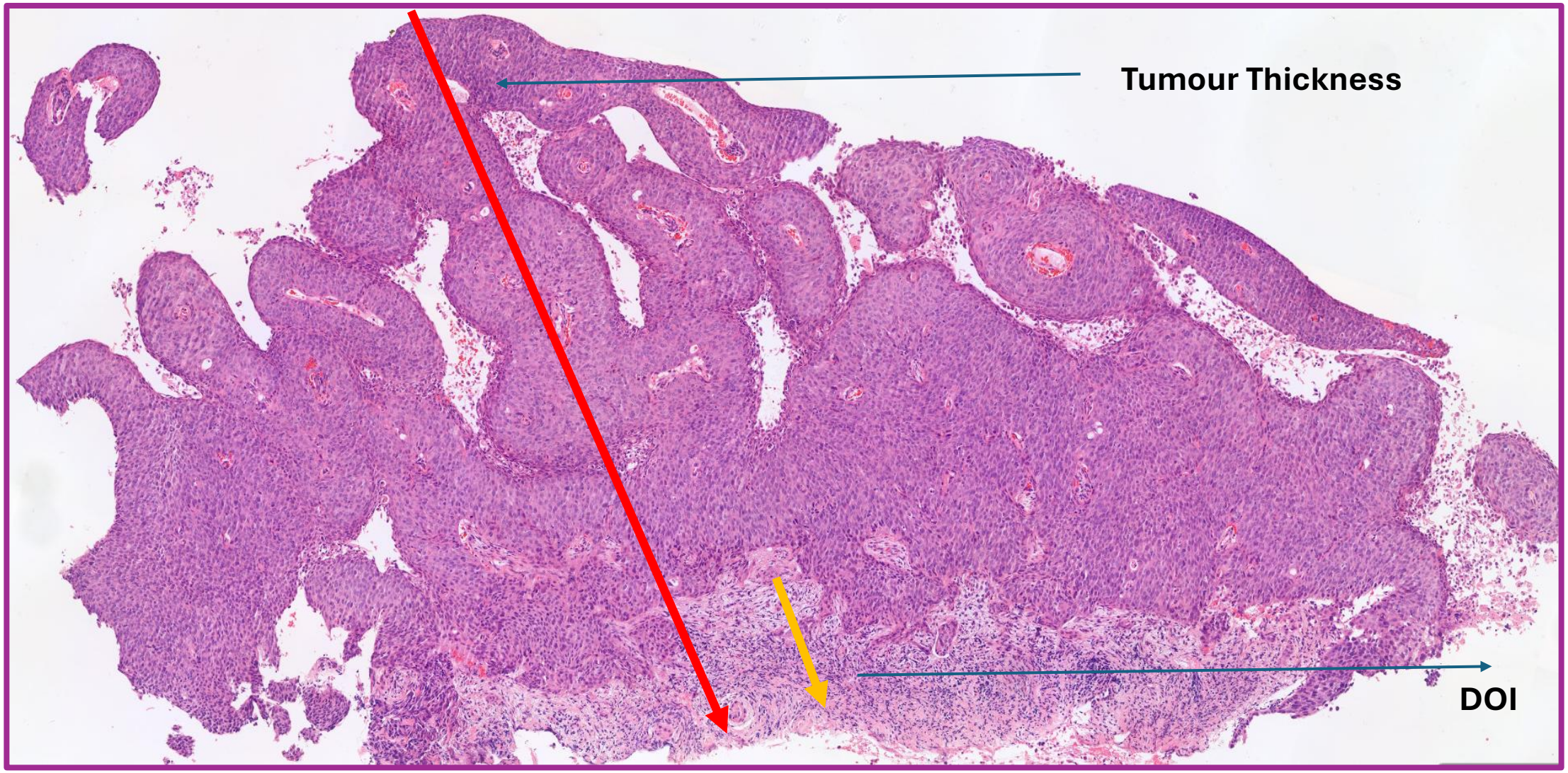


Exophytic Tumour

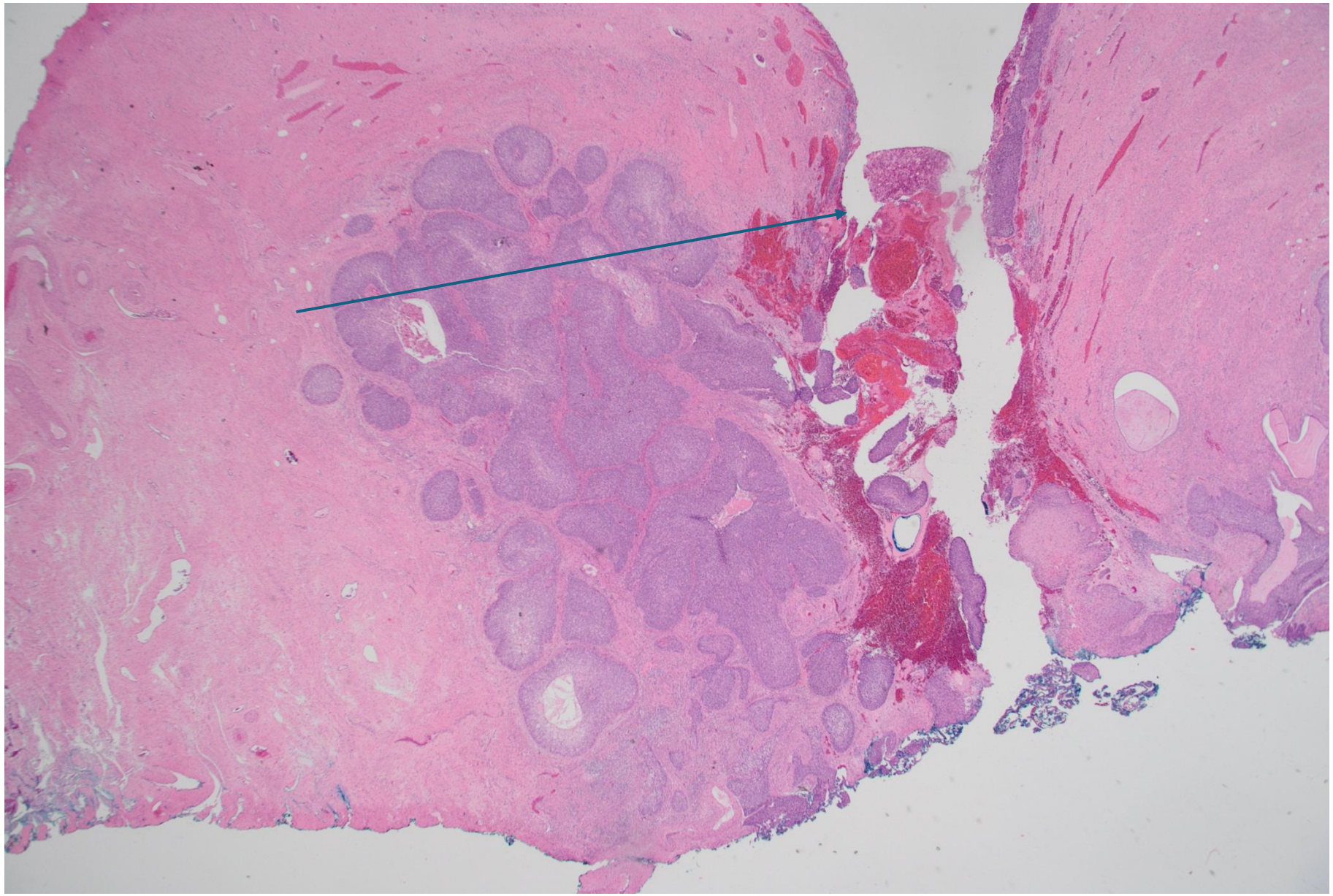




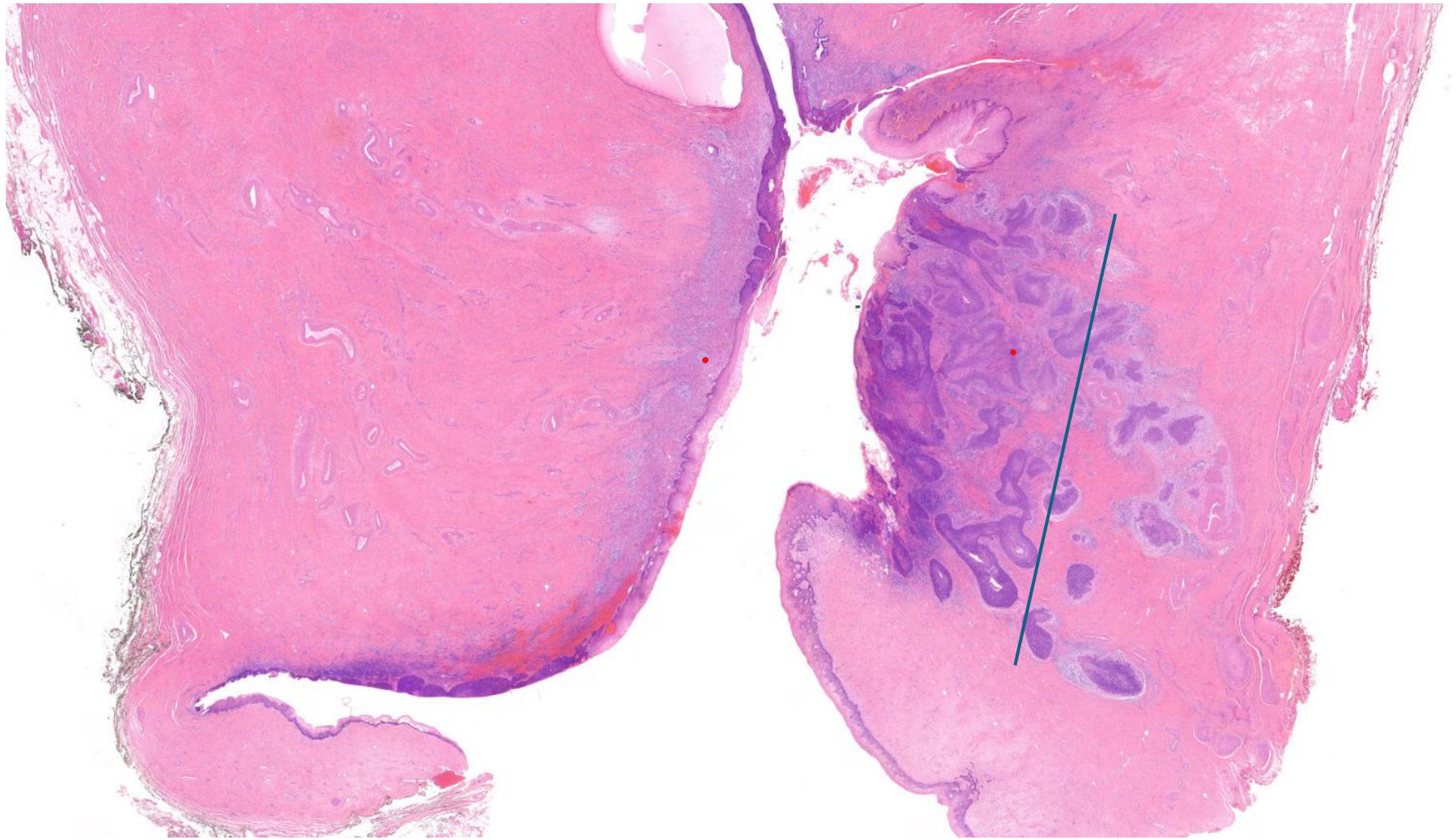
- **Tumour thickness** should be measured.
- From the surface of the tumour to the deepest point of invasion
- Should be clearly stated on the pathology report along with the reason

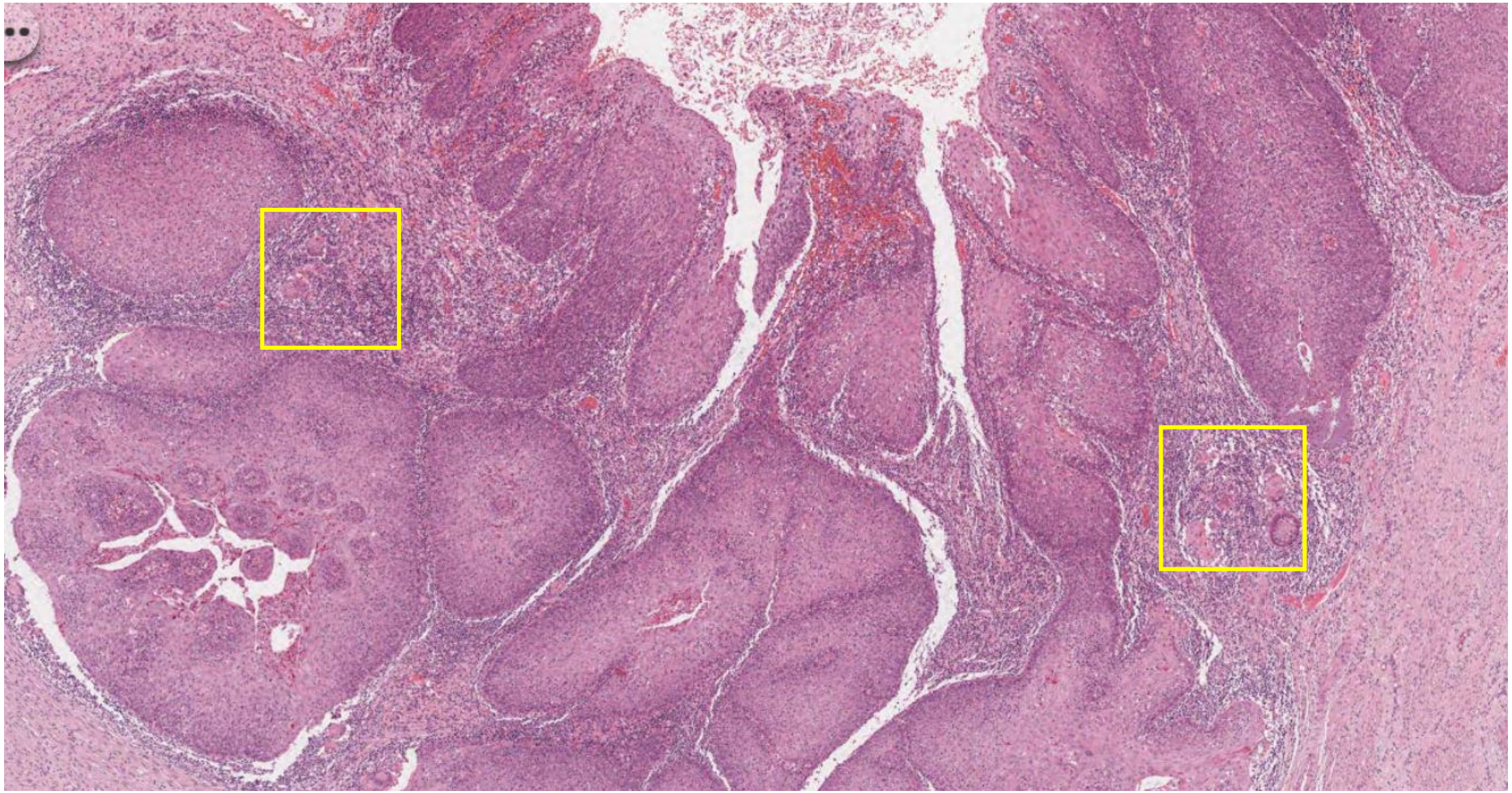

Tumour Thickness
DOI

Ulcerated tumour



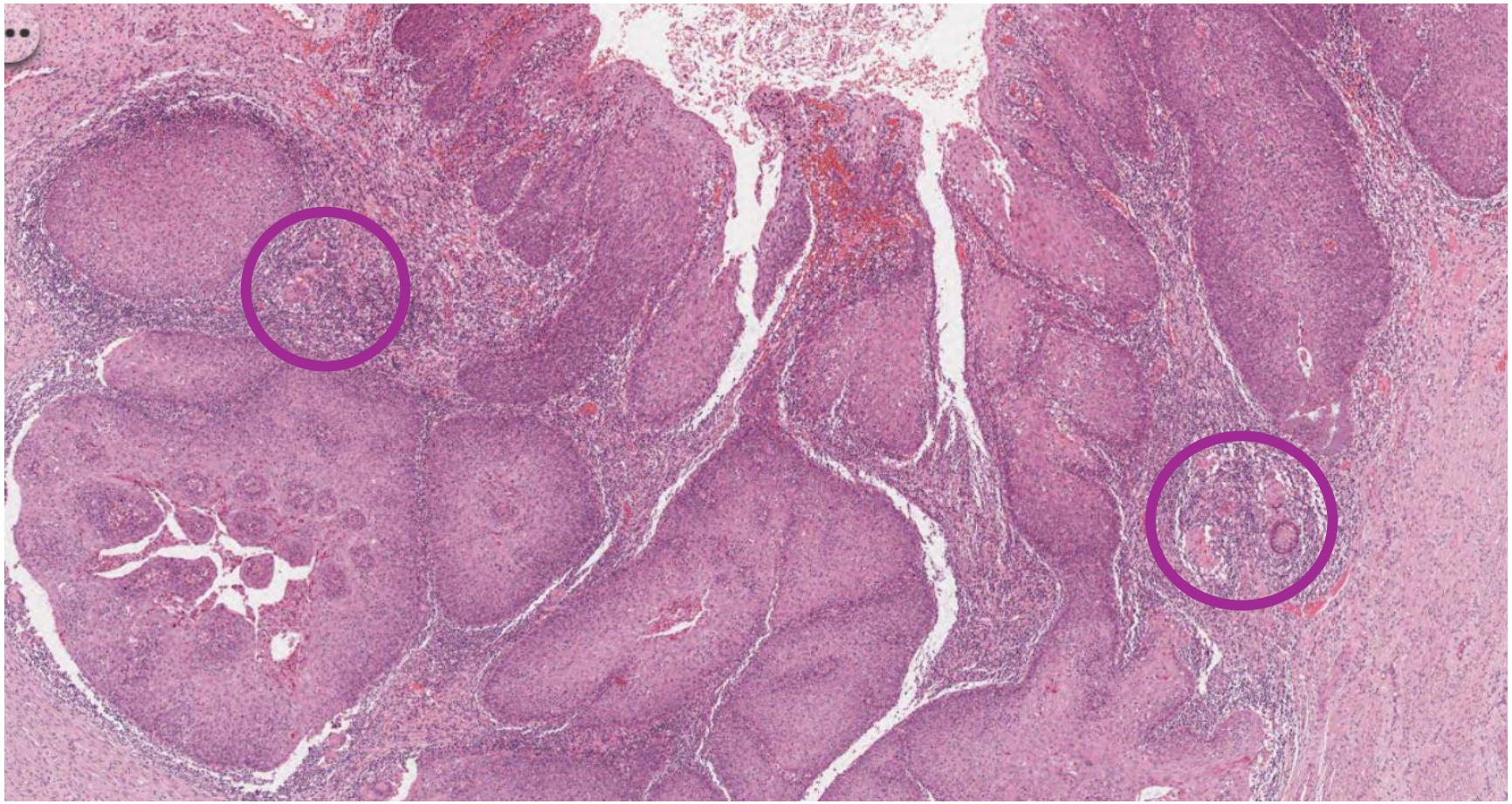
Horizontal measurement





Virtual Pathology Leeds

Multifocal Tumour



Leeds virtual pathology

Multifocal IA1 Carcinoma- ICCR guidance

- If foci of invasion are separated by blocks of uninvolved cervical tissue (Examine multiple levels to confirm).
- If foci of invasion are located on separate cervical lips
- If foci of invasion are situated far apart from each other in the same section (at least 2mm apart- arbitrary!) multiple levels .
- Measure each focus individual and stage according to the DOI of the deepest focus

- Multifocality in FIGO Stage IA1 cervical squamous carcinomas has been reported to be between 12% and 25%
- Studies have shown prognosis comparable to 1A1 tumours
- Potential to avoid radical surgery where fertility preservation is desired.

Multiple specimens

Prior cone/ Loop- ICCR Recommendations

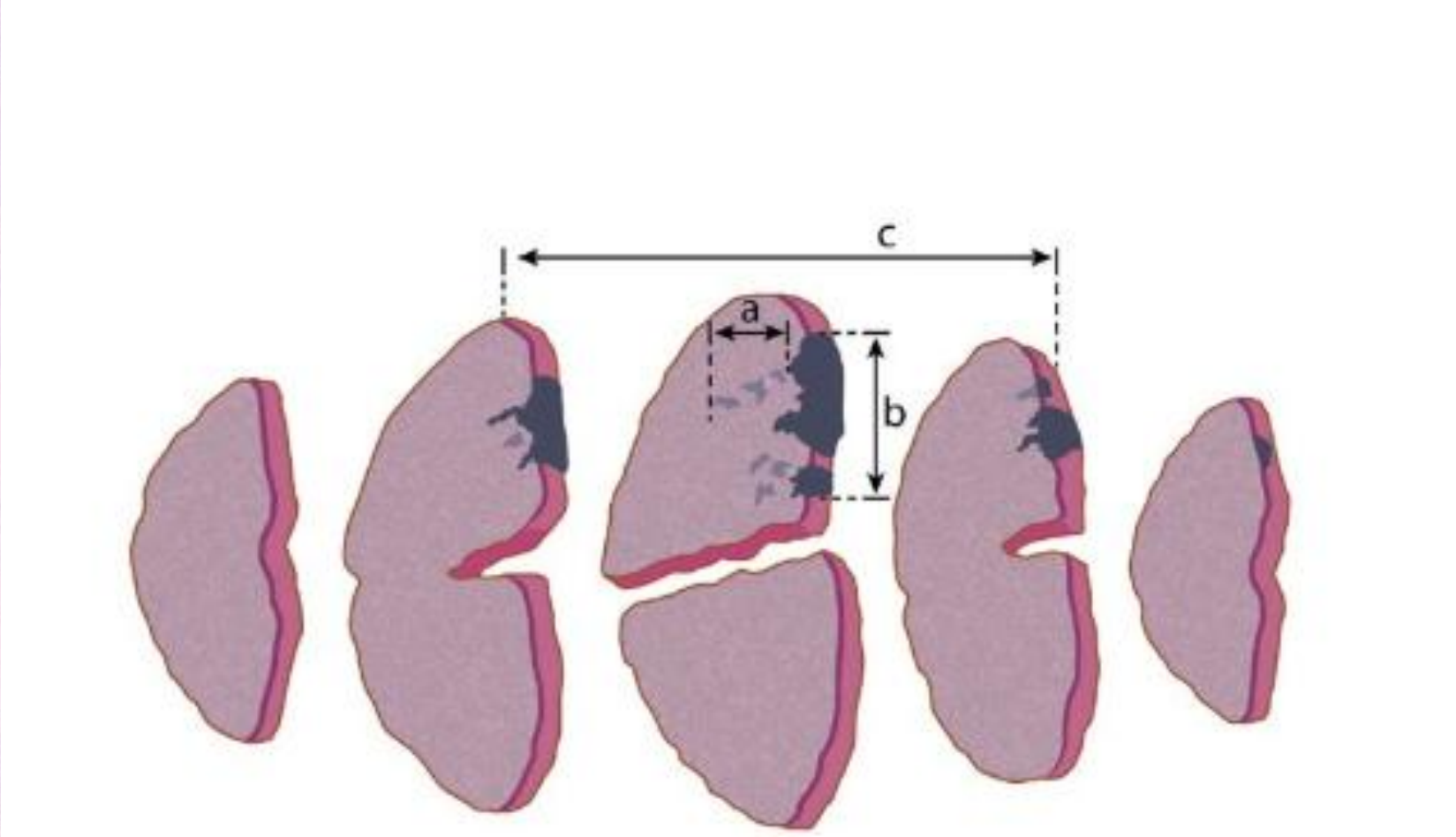
- Add maximum horizontal dimension of tumour in initial cone/ loop and maximum horizontal dimension of tumour in final cone/ loop/ hysterectomy/ trachelectomy together; may result in overestimation
- Maximum depth of invasion (in cone/ loop or hysterectomy/ trachelectomy) is taken as maximum depth of invasion; do not add together
- Communication between pathology and colposcopy teams vital.
- MDT discussion recommended.

Tumour measurements

- Largest measure of horizontal extent and the depth of invasion should be measured **in millimetres** for all tumours
- **Do not** give separate microscopic and gross measurements
- Measurements in any prior specimens should be considered when estimating the final dimension
- When margins are involved- use ‘at least’ for the size

- **Avoid term microinvasive carcinoma.**
    - Confusing term
    - Does not appear in FIGO staging system

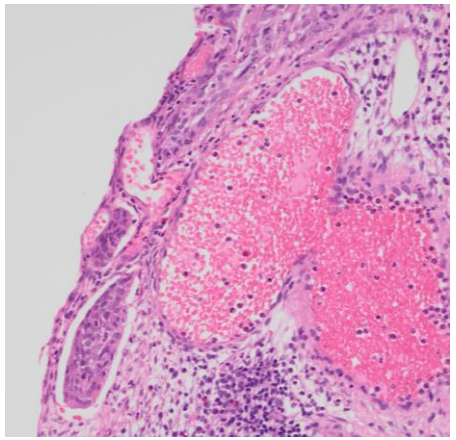
Tumour measurement (ICCR diagram)



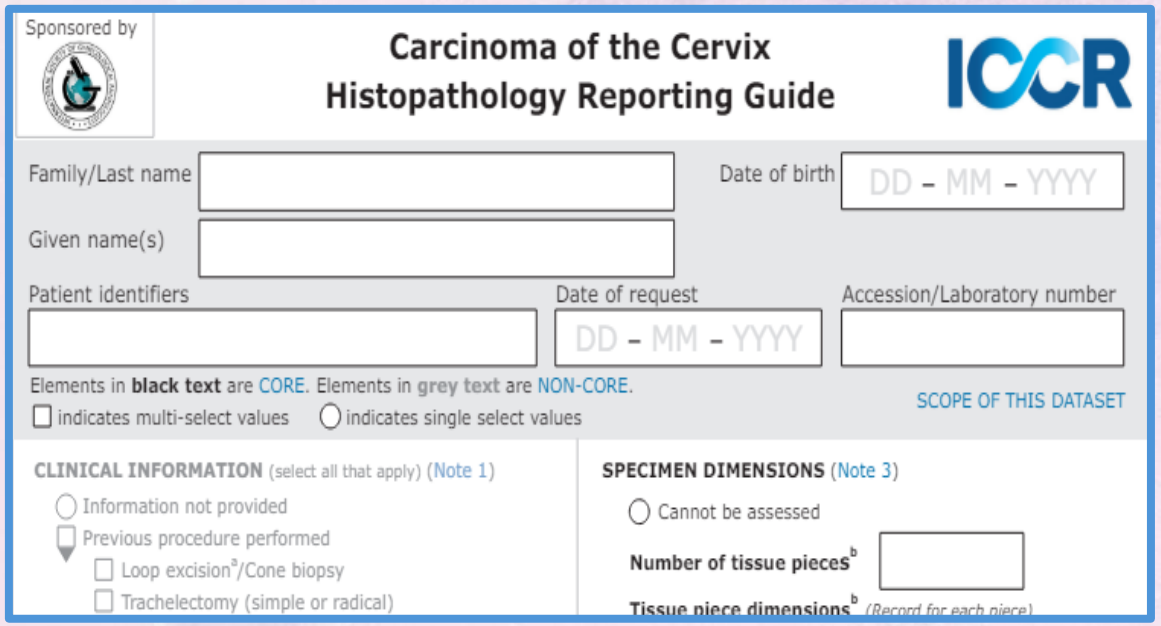
Tumour should be measured in two dimensions.

LVSI

- Does not affect tumour stage
- Adverse prognostic feature in early-stage cervical cancer
- May be seen even in small cancers
- Influence management in early-stage cancers



Pathology reporting of cervical carcinoma



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Carcinoma of the Cervix Histopathology Reporting Guide

ICCR

Family/Last name

Date of birth DD – MM – YYYY

Given name(s)

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in grey text are NON-CORE.

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (select all that apply) (Note 1)

◯ Information not provided

☐ Previous procedure performed

☐ Loop excision[a]/Cone biopsy

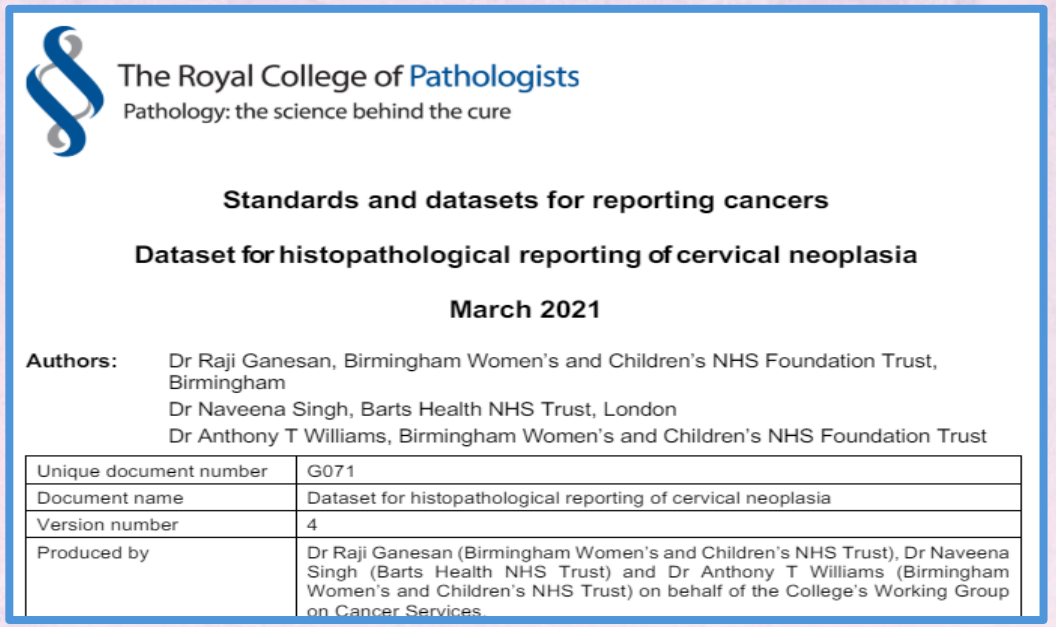
☐ Trachelectomy (simple or radical)

SPECIMEN DIMENSIONS (Note 3)

◯ Cannot be assessed

Number of tissue pieces[b]

Tissue piece dimensions[b] *(Record for each piece)*



The Royal College of Pathologists

Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for histopathological reporting of cervical neoplasia

March 2021

Authors: Dr Raji Ganesan, Birmingham Women's and Children's NHS Foundation Trust, Birmingham
Dr Naveena Singh, Barts Health NHS Trust, London
Dr Anthony T Williams, Birmingham Women's and Children's NHS Foundation Trust

Unique document number	G071
Document name	Dataset for histopathological reporting of cervical neoplasia
Version number	4
Produced by	Dr Raji Ganesan (Birmingham Women's and Children's NHS Trust), Dr Naveena Singh (Barts Health NHS Trust) and Dr Anthony T Williams (Birmingham Women's and Children's NHS Trust) on behalf of the College's Working Group on Cancer Services

ICCR Carcinoma of cervix dataset 5th edition 2023

https://www.iccr-cancer.org/datasets/published-datasets/female-reproductive/carcinomas-of-the-cervix/

- Incorporates **WHO 2020** classification of cervical cancers
- Incorporates **2018 FIGO** staging (includes 2019 revision)

Dataset for histopathological reporting of cervical neoplasia 2021

Summary

- Expansile crypt involvement /HIgh risk CIN3 –frequently associated with invasion – DO LEVELS

- WHO 2020 SCC classification -based on HPV association
  Ancillary test, minimum p16,recommended where accessible

- Grading SCC is not prognostically relevant, not a core data item

- Tumour measurement (DOI, max dimension) in early-stage cancers critical for patient management
  Special scenarios – Exophytic, ulcerated, multifocal tumours

Questions?

POLL- Assign an appropriate FIGO stage

SCC- Horizontal dimension 14mm , depth of invasion 4.5mm, LVSI present.

A.FIGO 1A1

B.FIGO 1A2

C.FIGO 1B1

D.FIGO 1B2

E.FIGO 1B3