

Difficult Cervical Invasive lesions, and mimics

A/P Diane Kenwright

Key learning:

- Using the WHO 2020 classification
- Using the Silva classification
- Invasive vs in situ
- Special types you must recognise
- Mimics of carcinoma

Before you begin...

Watch these videos

[Difficult Diagnoses in Cervical Histopathology – Part 1 Squamous](https://vimeo.com/294714043/c9c120ea72)

12 minutes

<https://vimeo.com/294714043/c9c120ea72>

[Difficult Diagnoses in Cervical Histopathology – Part 2 Glandular](https://vimeo.com/294714095/0706b11e27)

23 minutes

<https://vimeo.com/294714095/0706b11e27>

Endocervical adenocarcinoma classification: WHO 2014 and IECC 2018/WHO 2020

WHO 2014	IECC 2018/WHO 2020
Endocervical adenocarcinoma, usual type	HPV-associated endocervical adenocarcinoma Usual type Mucinous type (NOS, intestinal, signet-ring cell, ISMC) Adenocarcinoma NOS
Mucinous carcinoma NOS	
Mucinous carcinoma, gastric type	
Mucinous carcinoma, intestinal type	
Mucinous carcinoma, signet ring cell type	
Villoglandular carcinoma	
Mesonephric carcinoma	
Serous carcinoma	
Clear cell carcinoma	
Endometrioid carcinoma	
Adenocarcinoma NOS	HPV-independent endocervical adenocarcinoma Gastric type Clear cell type Mesonephric type Endometrioid type Adenocarcinoma NOS

International Endocervical Adenocarcinoma
Criteria and Classification (IECC)

*A New Pathogenetic Classification for Invasive
Adenocarcinomas of the Endocervix*

Simona Stolnicu, MD, Iulia Barsan, MD,* Lien Hoang, MD,† Prisha Patel, MPH,‡
Cristina Terinte, MD,§ Anna Pesci, MD,|| Sarit Aviel-Ronen, MD,¶ Takako Kiyokawa, MD,#
Isabel Alvarado-Cabrero, MD,** Malcolm C. Pike, PhD,‡ Esther Oliva, MD,††
Kay J. Park, MD,‡ and Robert A. Soslow, MD,‡*

**HPVA
HPV-Associated**

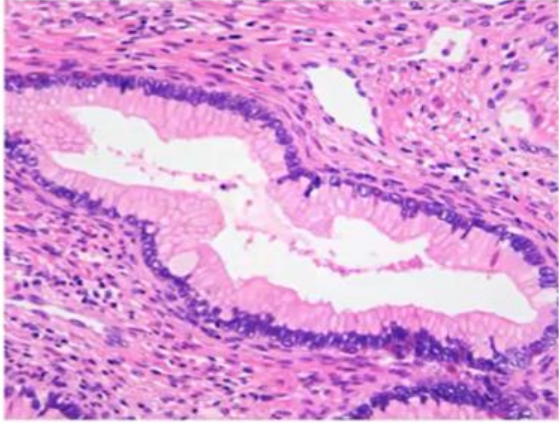
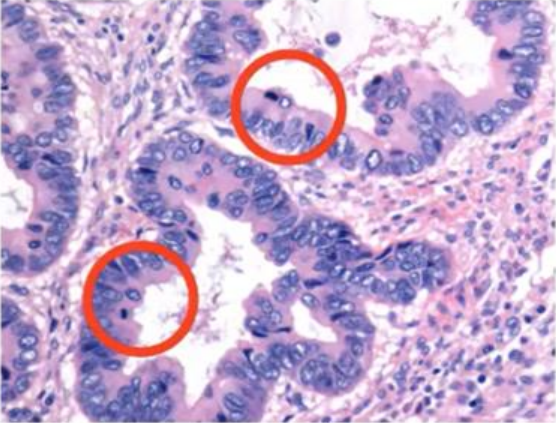


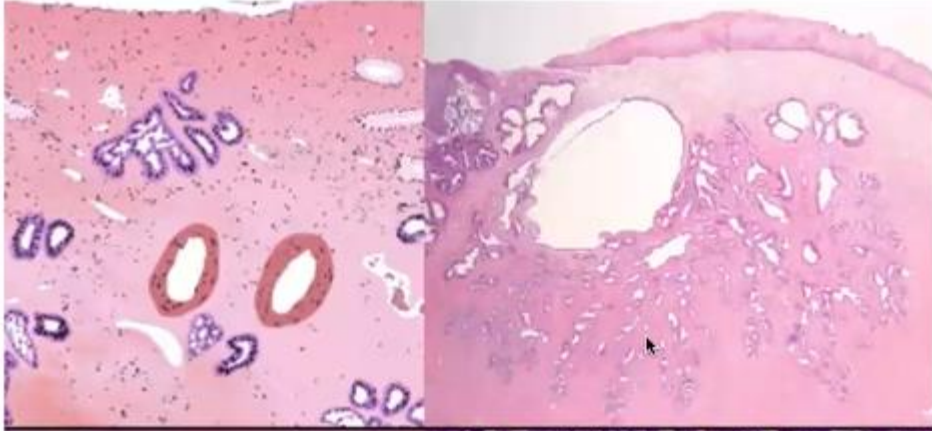
Apical mitotic figures and apoptotic bodies at scanning magnification

**HPVI
HPV-Independent**



No easily identified/absent mitoses and apoptosis at scanning magnification





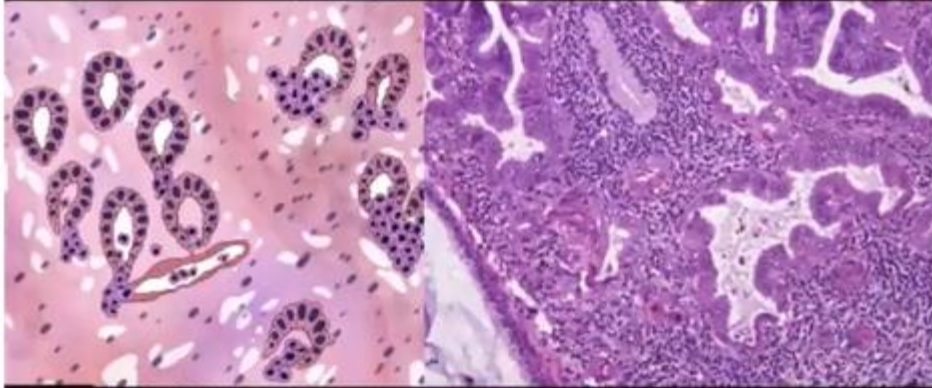
Silva A

No destructive stromal invasion

Usually preserved lobular architecture

Well-demarcated glands with rounded contours

No LVI



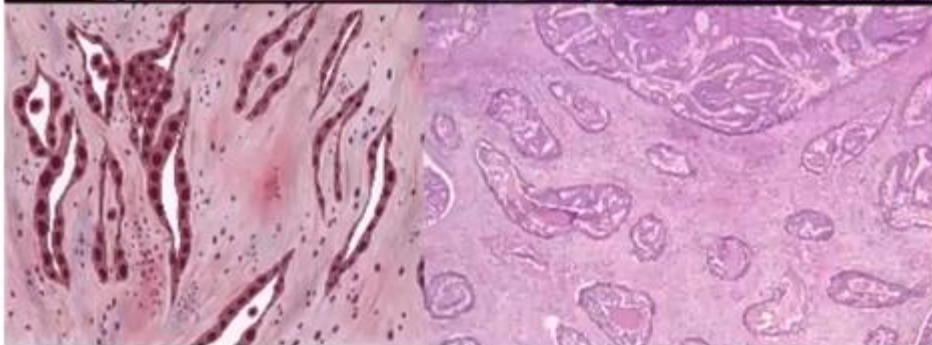
Silva B

Early (limited) destructive stromal invasion

Less than 4 x field, 5mm in diameter

Similar architecture to pattern A at low-power magnification

+/- LVI



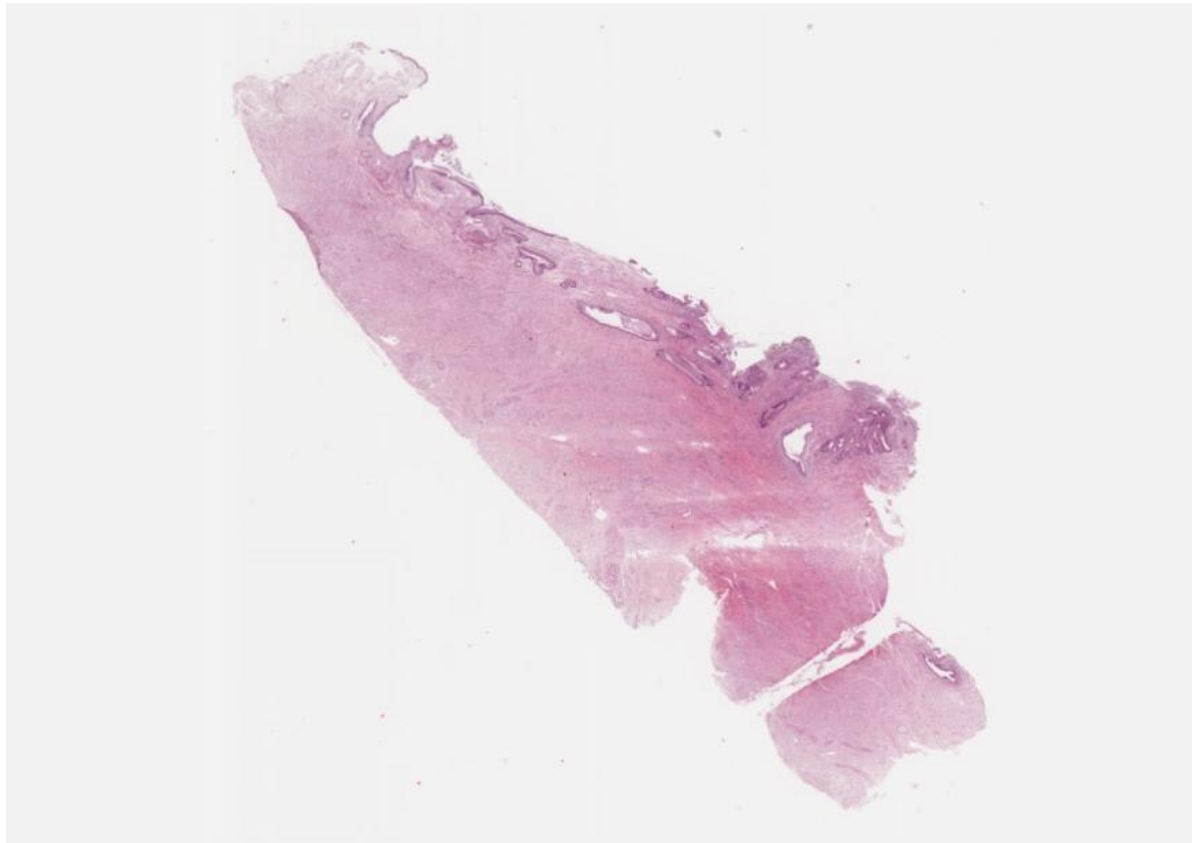
Silva C

Extensive and diffuse destructive invasion

Extensive desmoplastic stromal response

High nuclear grade; +/- LVI

<https://virtual.rcpaqap.com.au/publiclinklauncher/SectraUniviewLaunch?accessString=qjdaCQQihi%2BkRqQ%2BzAnfpqlf5t6avQvb3orzx0G7OEVl8Alm5wpgCl2cDA7GlbwE6vDM1tl8BN%2Fp6UexUvmV%2FzQapEEMymhl18xjSssn9JayvSzmdu5Aweq5FRJ5CDaqEkdTMZmXsOLmciRf0RMQCOhloIxMfqUjFhnR%2FUqo4k9%2Be9GvNI1BqwjmEwrUWTCdZGZdfvFUAXQ%3D>



Were any of the indicators of it being a Silva A cervical adenocarcinoma present?

Does it exceed the distribution and density of normal endocervical glands?

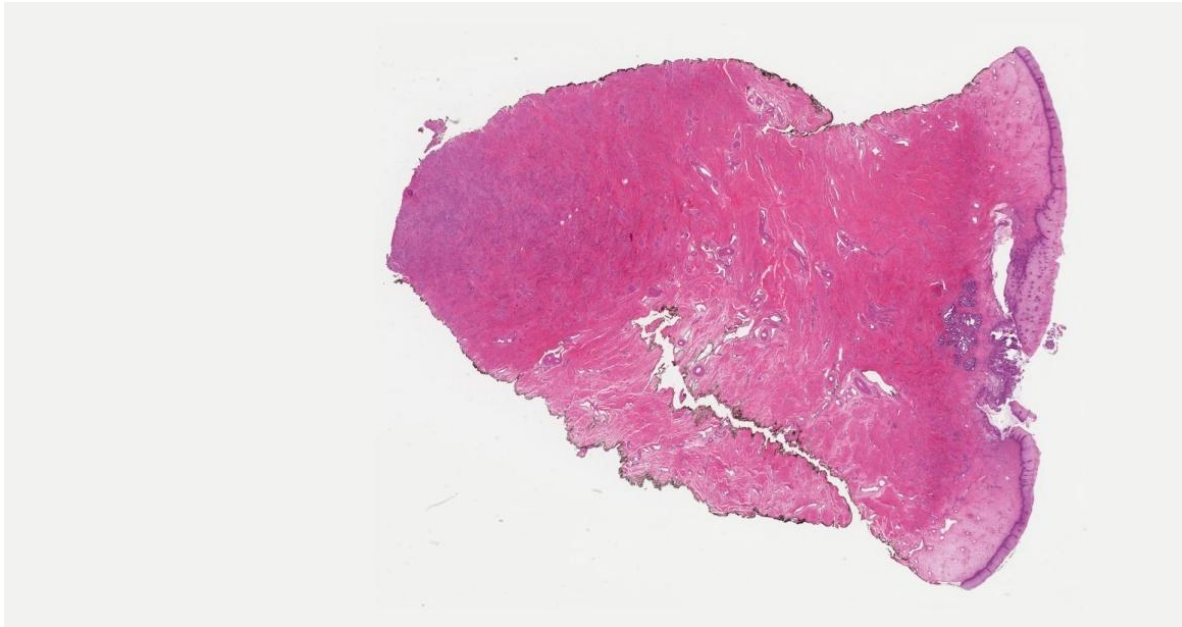
Is it expansile?

Either lymphocytes or stromal reaction present?

Squamoid change? Elastic sign?
Large vessels?

AIS. HPV- associated

<https://virtual.rcpaqap.com.au/publiclinklauncher/SectraUniviewLaunch?accessString=qjdaCQQihi%2BkRqQ%2BzAnfpqIf5t6avQvb3orzx0G7OEVl8Alm5wpgCI2cDA7GlbwE6vDM1tl8BN%2Fp6UexUvmV%2F%2FykdfvZJAbgk7hGp6qfMUD6eoOnPf%2BALexaWrEciMBKDmi%2BxRt5x5BRbL5p7qq98xhQSt1oyUvP1lBQWLQ7GDHrB6iUGPa%2Bb66cl5htnhclgb2qXBk%2Fj6s%3D>



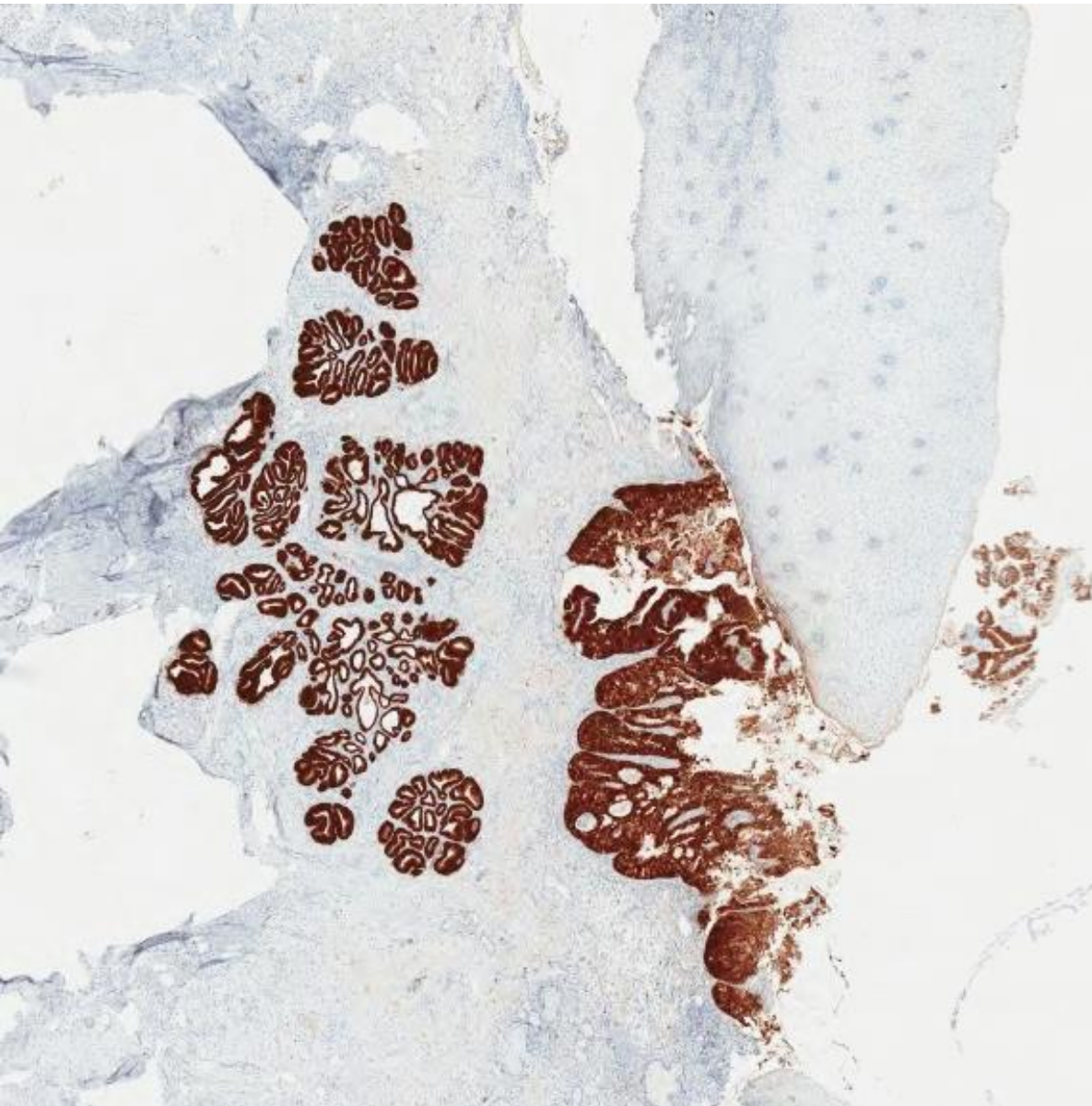
Were any of the indicators of it being a Silva A cervical adenocarcinoma present?

Does it exceed the distribution and density of normal endocervical glands?

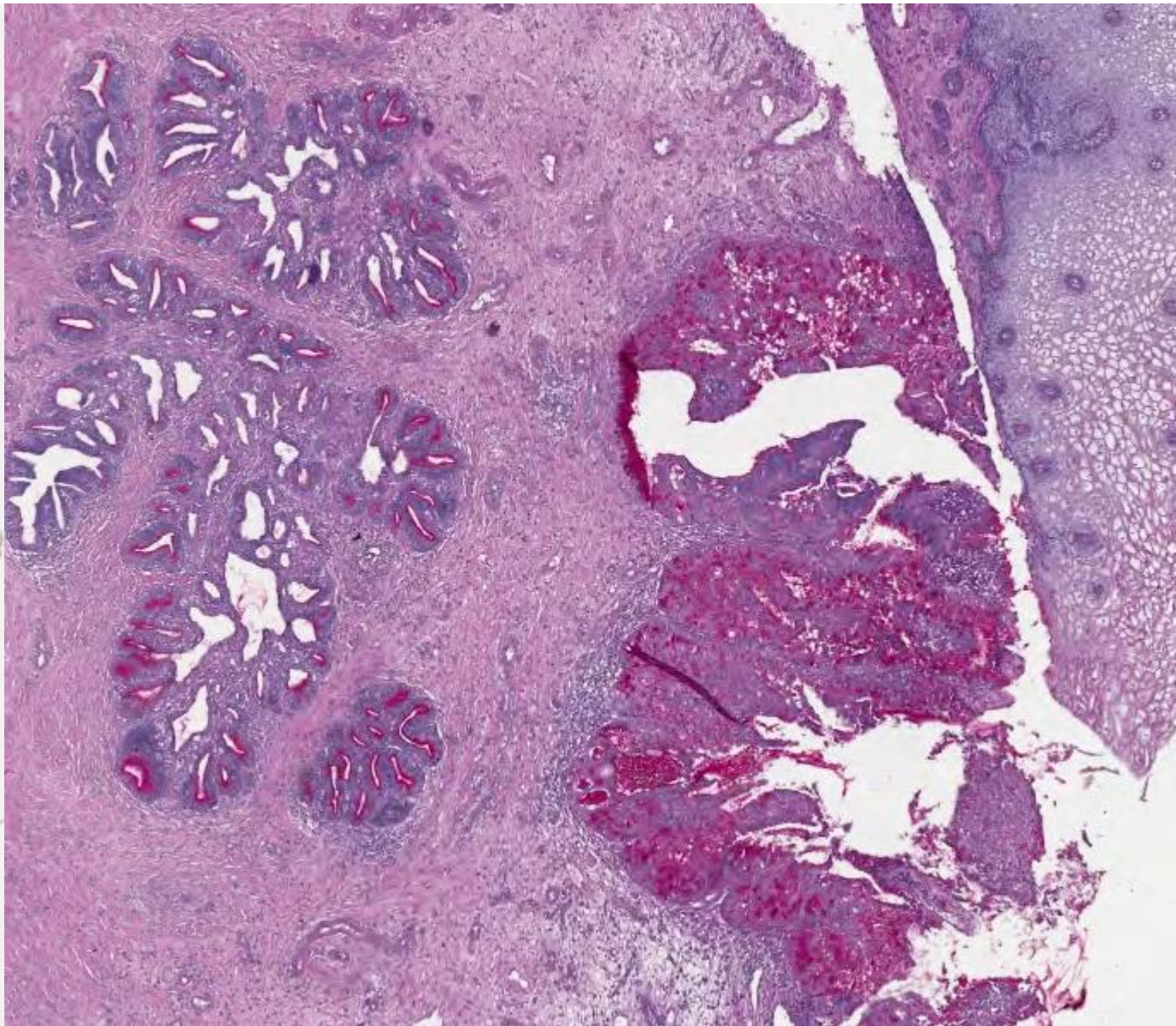
Is it expansile?

Either lymphocytes or stromal reaction present?

Squamoid change? Elastic sign?
Large vessels?



p16

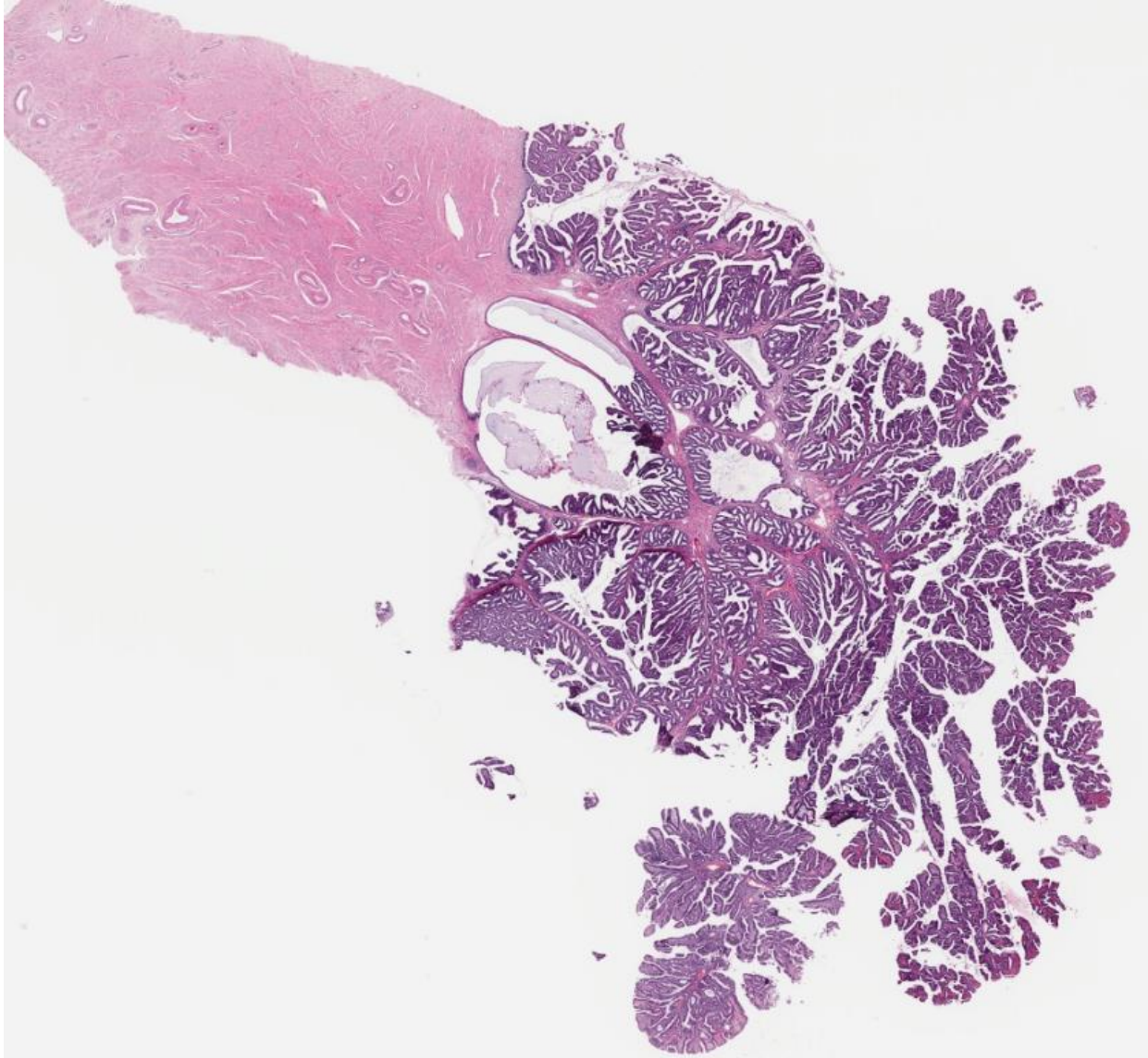


PAS

Cervical adenocarcinoma, HPV associated,
usual type, Silva pattern A.

SMILE in overlying epithelium

<http://rosai.secondslide.com/sem1174/sem1174-case6.svs>



Diagnosis?

Silva pattern?

Stains?

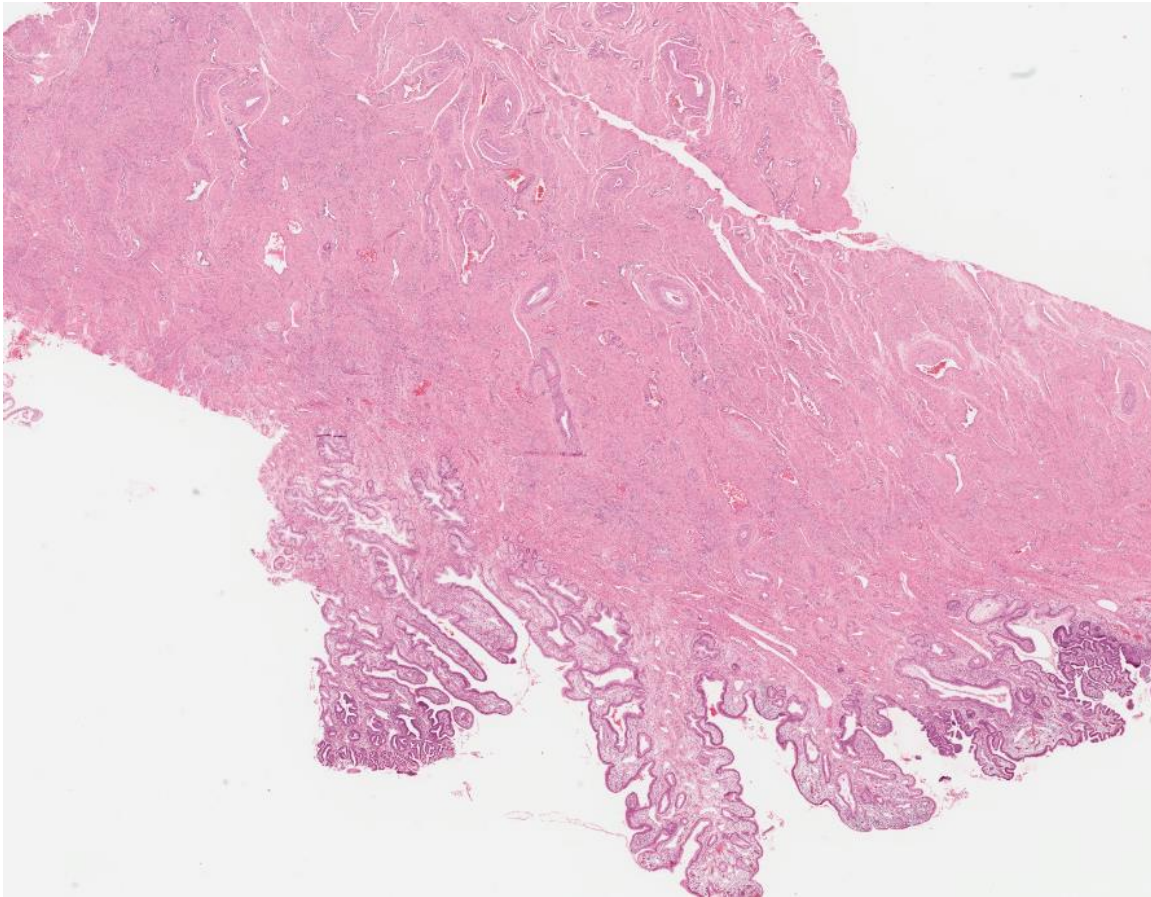
DDx?

Cervical adenocarcinoma, HPV associated,
usual type, Silva pattern A.

Villoglandular growth pattern

Do p16 (otherwise NOS)

<http://rosai.seconslide.com/sem349/sem349-case7.svs>



Were any of the indicators of it being a
Silva A cervical adenocarcinoma present?

Does it exceed the distribution and
density of normal endocervical glands?

Is it expansile?

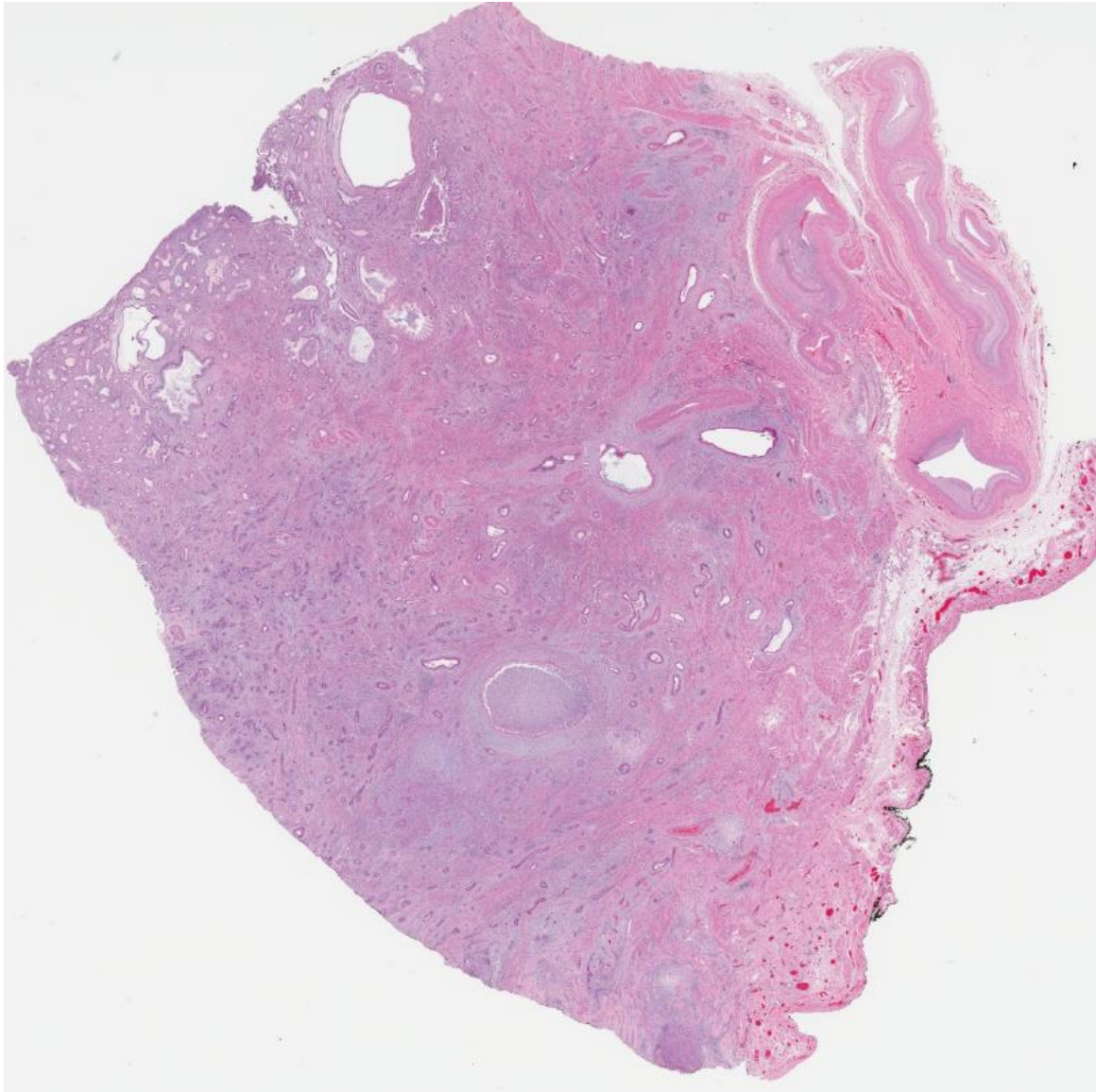
Either lymphocytes or stromal reaction
present?

Other signs?

Cervical adenocarcinoma, HPV associated,
usual type, Silva pattern A.

AIS in overlying epithelium

<http://rosai.seconslide.com/sem1161/sem1161-case2.svs>



Diagnosis?

Silva pattern?

Stains?

DDx

Cervical adenocarcinoma, HPV-I, Gastric type, Silva pattern C.

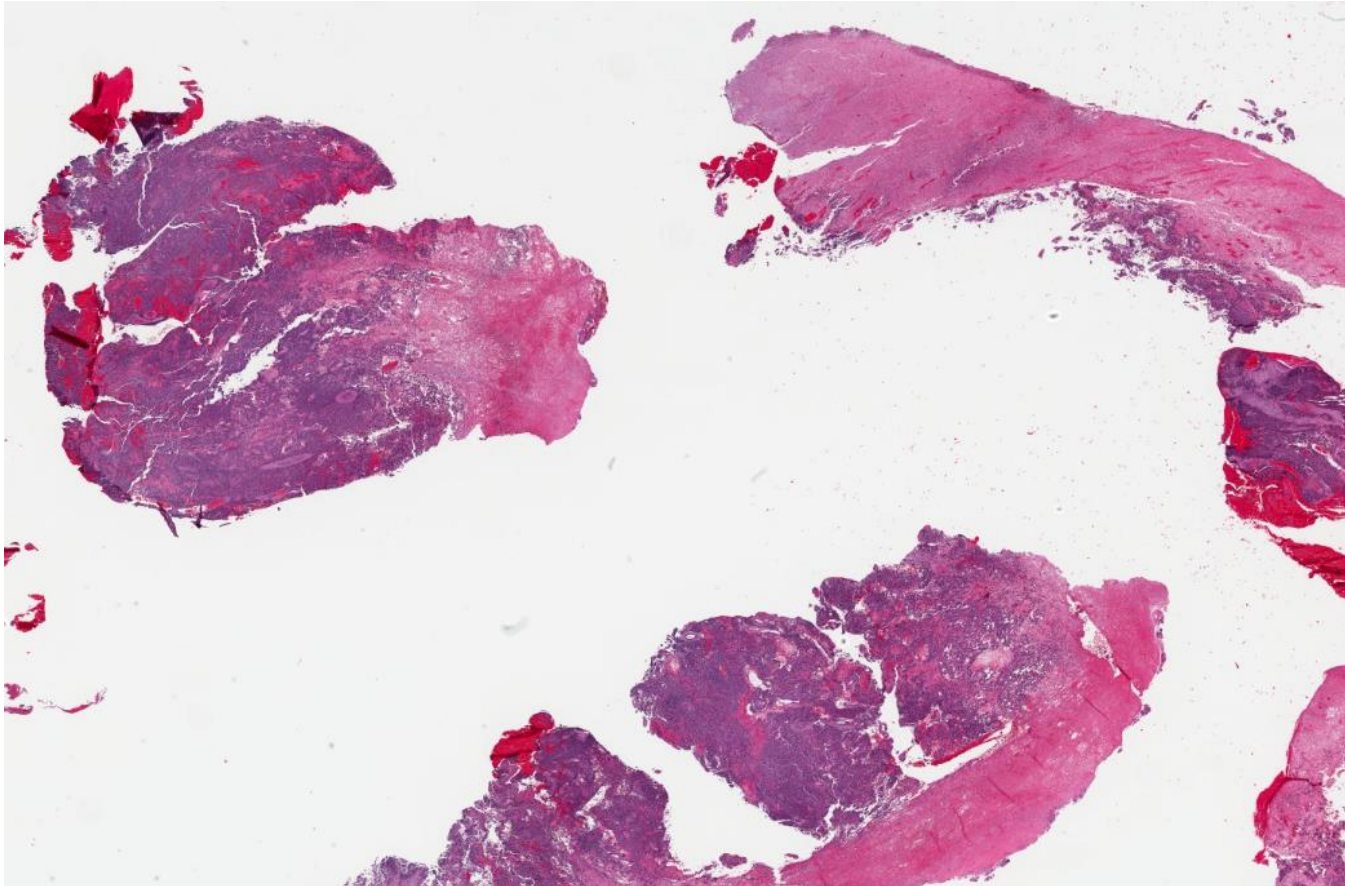
Do p16 (otherwise NOS)

? Gastric type – 1/3 are p16 positive, so do HPV – ISH if you think it is gastric and p16 positive.

MUC6 positive (anyone have this?)

DDx – Cervical adenocarcinoma, HPV-A mucinous type, NOS

<http://rosai.seconslide.com/sem1053/sem1053-case7.svs>



Diagnosis?

Silva pattern?

Stains?

DDx?

Cervical adenocarcinoma, HPV-A, small cell neuroendocrine type, Silva pattern C.

Do p16 (otherwise NOS)

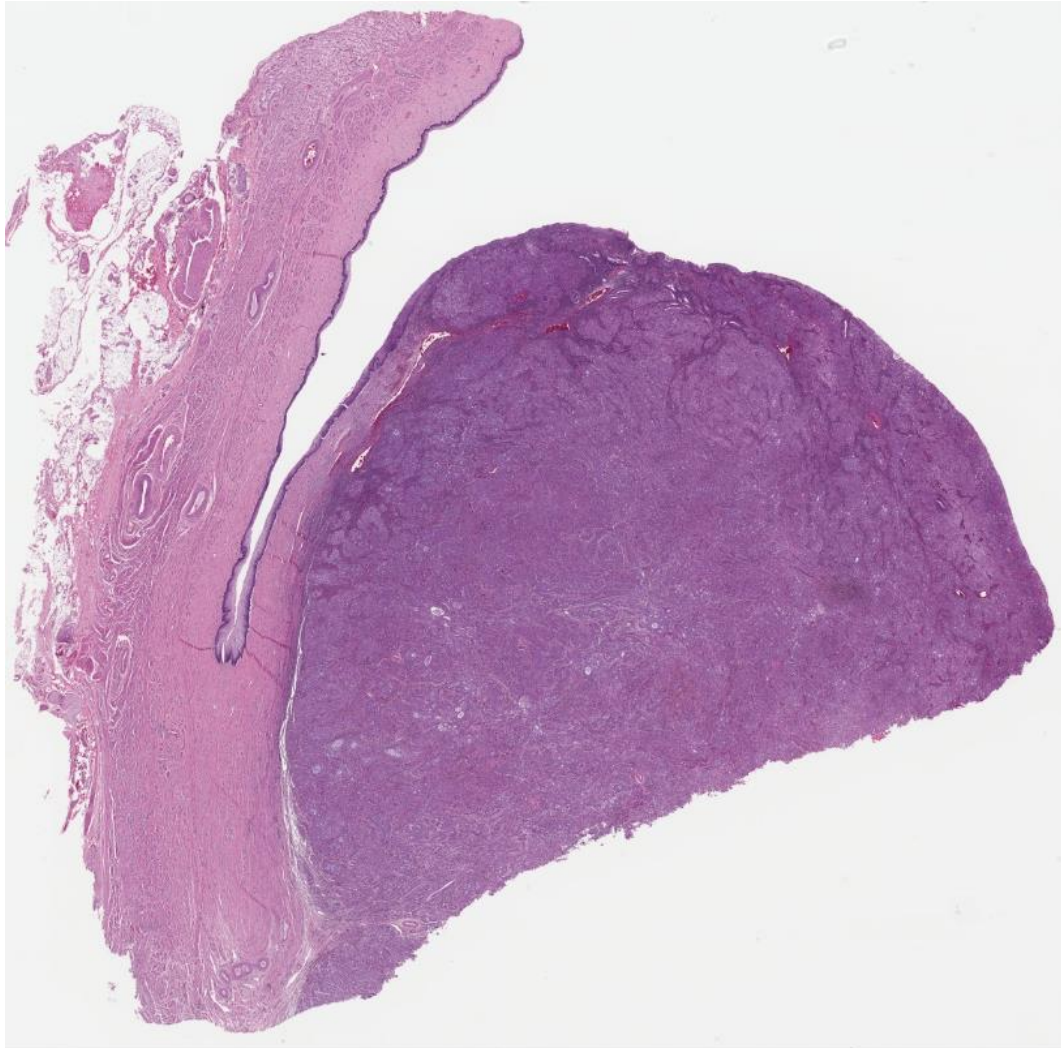
Small cell –p16 positive

Synaptophysin, chromogranin, CD56

DDx – Poorly differentiated SCC

Other small round blue cell tumours

<http://rosai.seconslide.com/sem1198/sem1198-case11.svs>



Diagnosis?

Silva pattern?

Stains?

DDx?

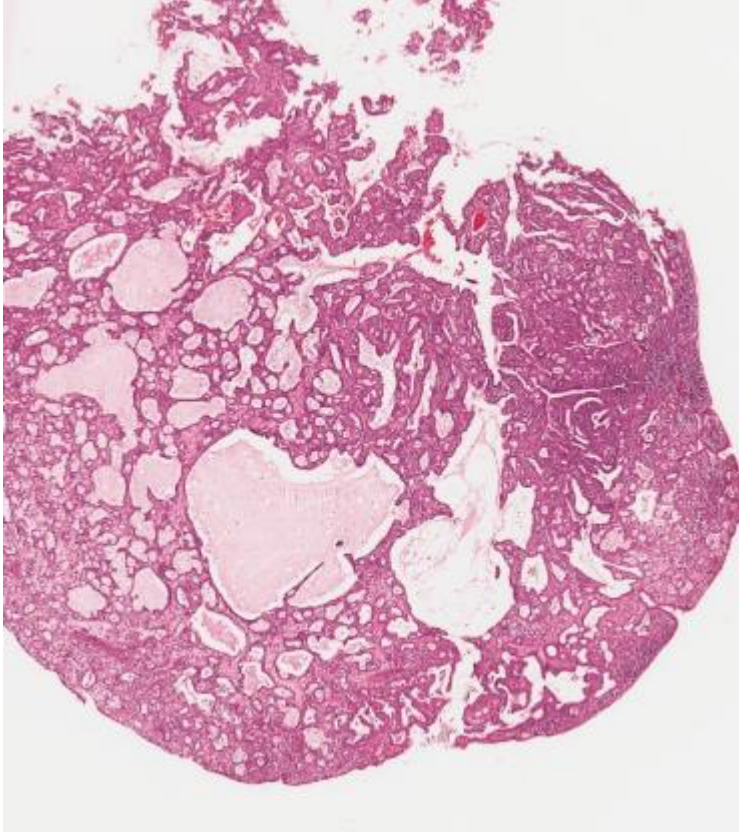
Cervical adenocarcinoma, HPV associated,
Mucinous type (SMILE), Silva pattern C.

Do p16 (otherwise NOS)

PAS

DDx adenosquamous – has distinct areas of
glands and SCC

<http://rosai.seconslide.com/sem333/sem333-case14.svs>



Diagnosis?

Silva pattern?

Stains?

DDx?

Usual type in situ adenocarcinoma- differential diagnosis

	In situ adenocarcinoma, HPV+	Tubal metaplasia/Other benign lesions
p16	+ (block-type)	- (non-block)
bcl2	-	+
ki67	high (>30%)	low (<10%)
Vimentin	-	+
ER/PR	-	+
CEA	+ cytoplasmatic	-/luminal

Microglandular hyperplasia

p16- patchy/negative

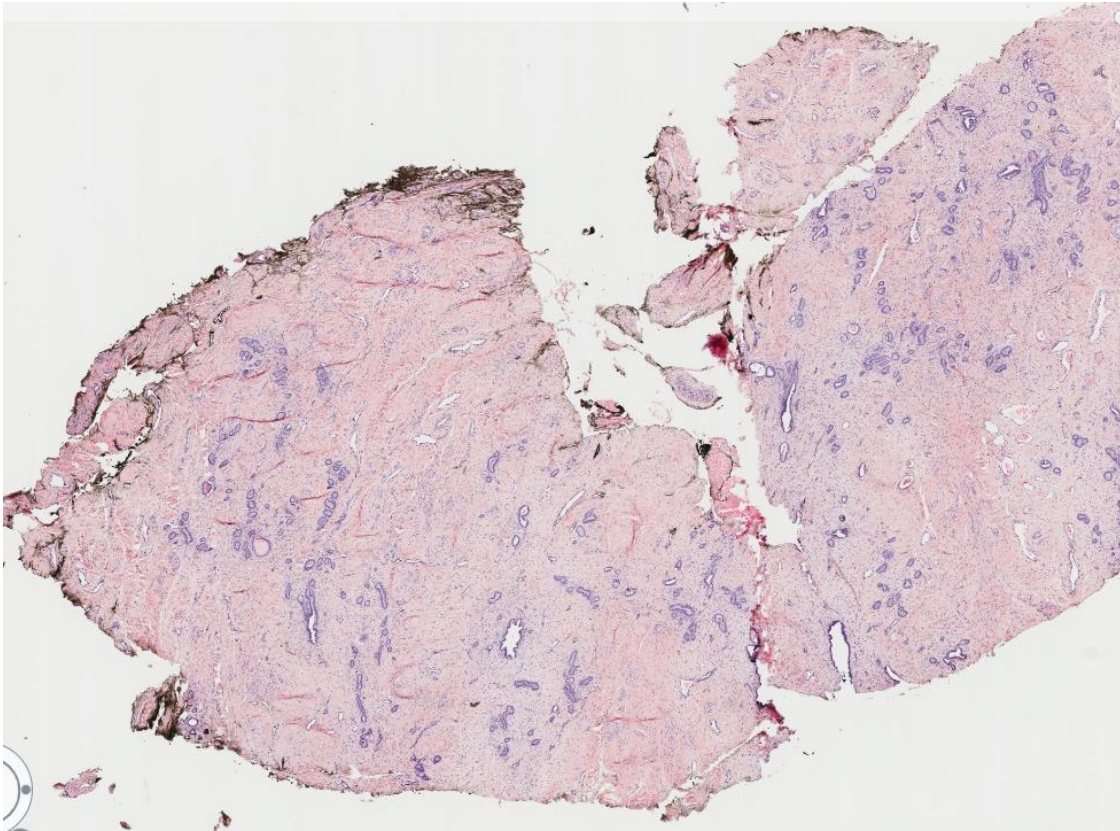
CEA negative (or confined to lumen), p63 positive in the basal cells, Ki67 <10%,

DDx Adenocarcinoma HPV-A

Adenocarcinoma HPV-I clear cell, endometrioid

ER +, PR -, Vim-, Napsin A -

<http://rosai.seconslide.com/sem926/sem926-case1.svs>



Diagnosis?

Silva pattern?

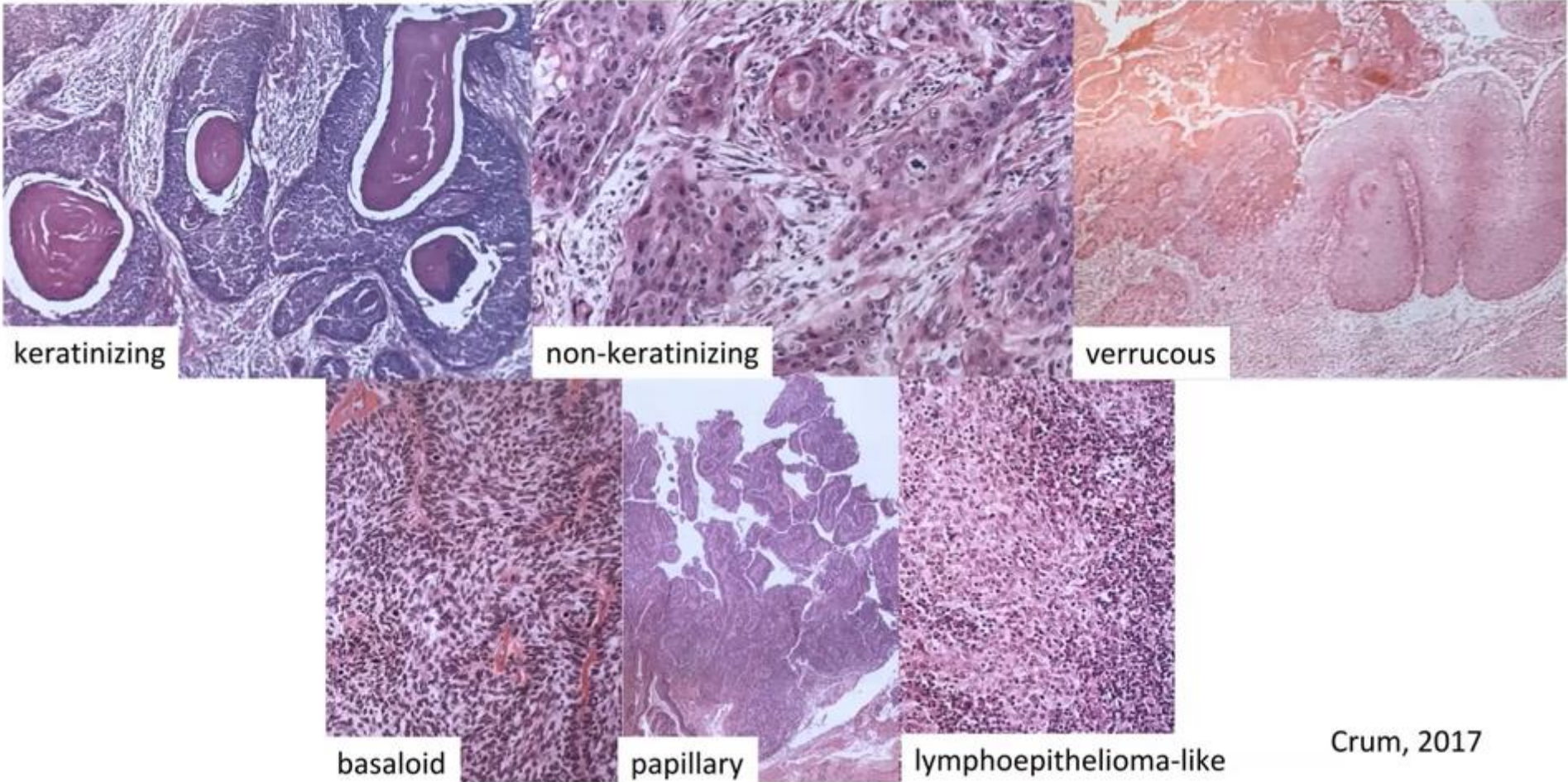
Stains?

DDx?

Comparison of WHO 2014 and 2020 classification for SCCs

2014 WHO classification	2020 WHO classification
<p>Squamous cell carcinoma usual type</p> <ul style="list-style-type: none">KeratinizingNon-keratinizing <p>Papillary</p> <p>Basaloid</p> <p>Warty</p> <p>Verrucous</p> <p>Squamotransitional</p> <p>Lymphoepithelioma-like</p>	<p>Squamous cell carcinoma, HPV-associated</p> <p>Squamous cell carcinoma, HPV-independent</p> <p>Squamous cell carcinoma, NOS</p>

HPVA SCC: histologic growth patterns (WHO, 2020)

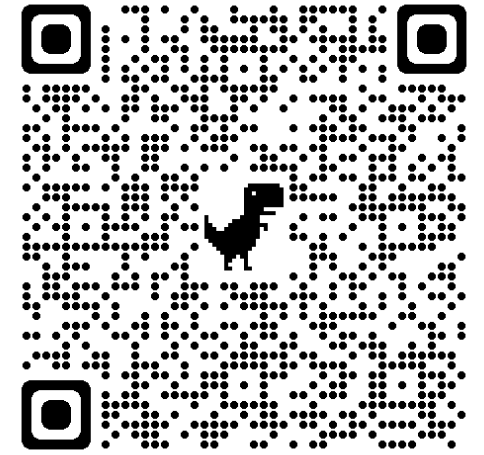
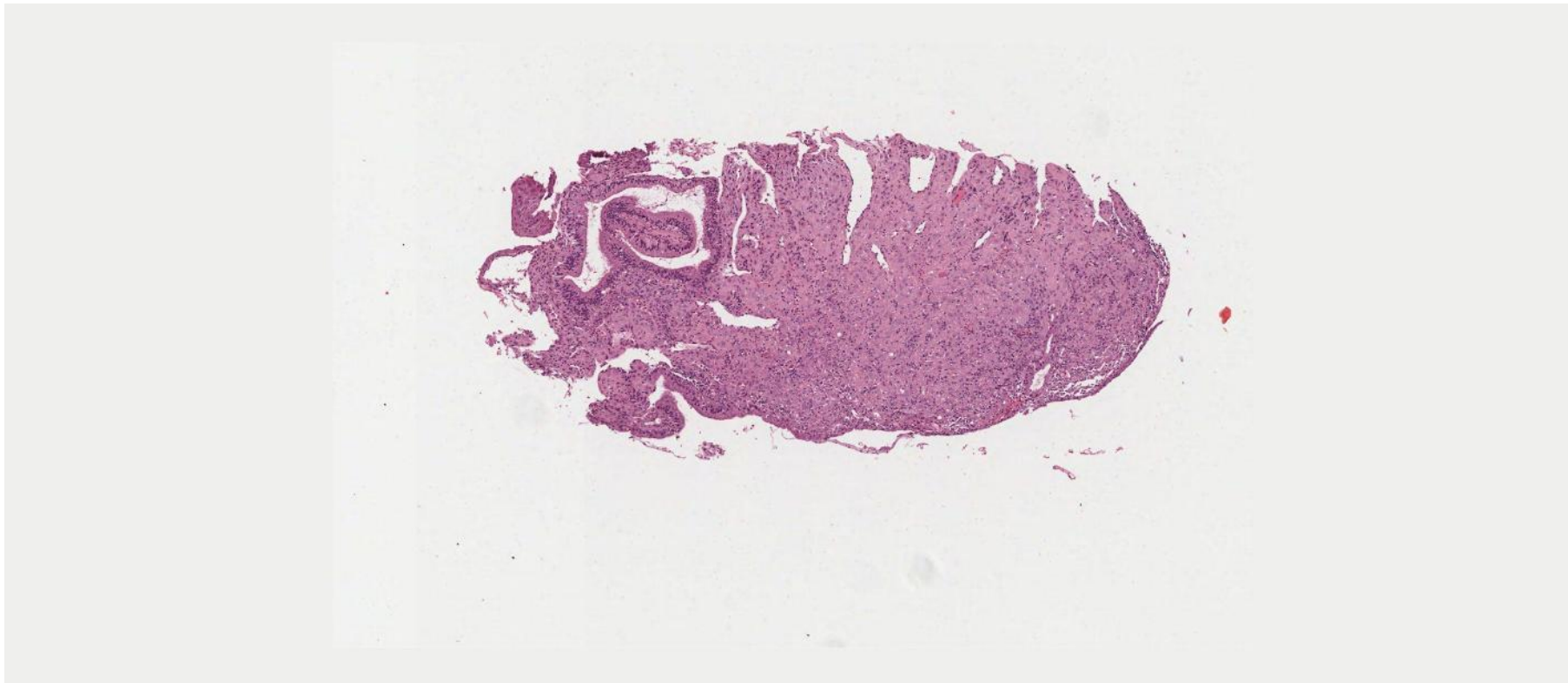


Crum, 2017

Grading is based on nuclear pleomorphism, size of nucleoli, mitotic activity and necrosis and does not correlate with prognosis

- Well differentiated: variably shaped and sized nests with **abundant keratin pearls, large cells with abundant eosinophilic cytoplasm** and well developed intercellular bridges, occasional mitoses, necrosis may be present
- Moderately differentiated: round to irregular and variably sized nests, cords and sheets, **focal keratinization**, large to medium sized and relatively uniform cells with indistinct cell borders, readily identifiable mitoses
- Poorly differentiated: small nests, cords and sheets and single cells, small cells with scant cytoplasm, hyperchromatic nuclei and brisk mitoses, **absent or rare keratinization**

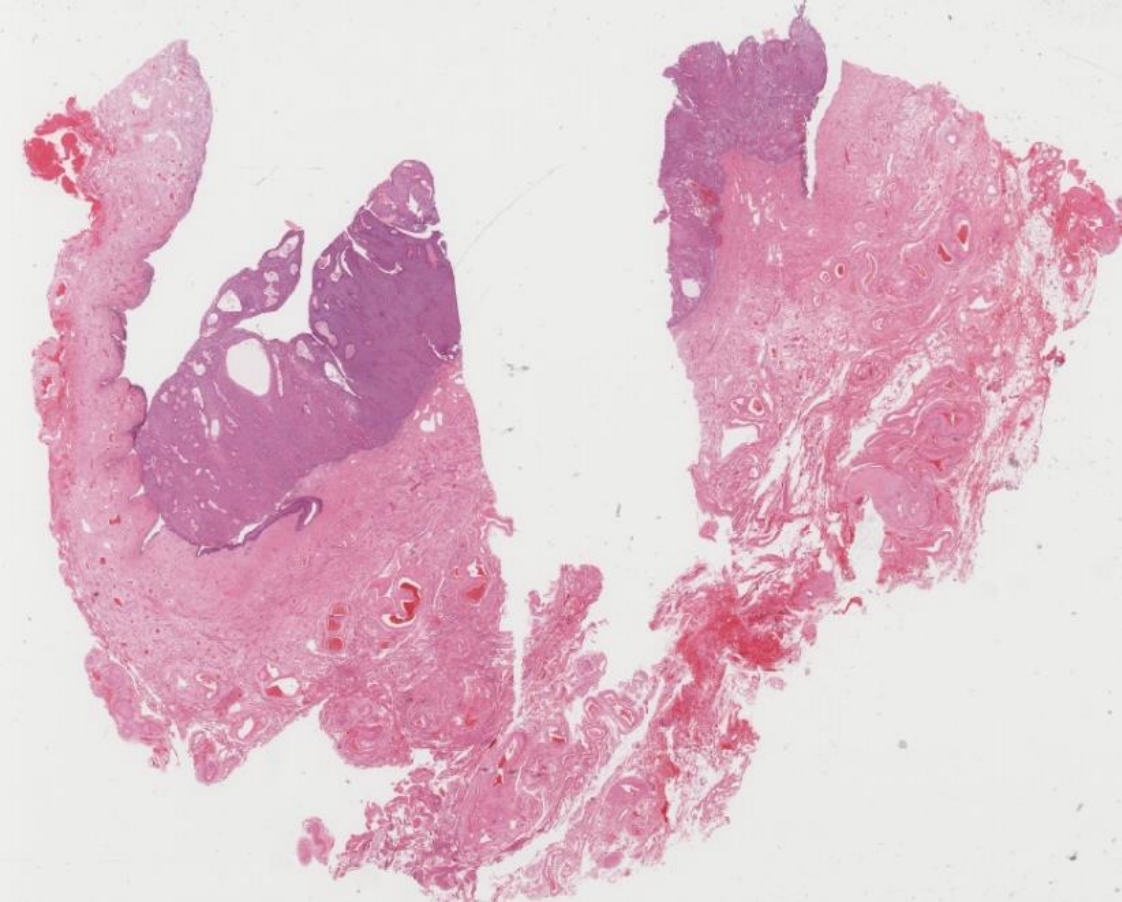
<https://virtual.rcpaqap.com.au/publiclinklauncher/SectraUniviewLaunch?accessString=qjdaCQQihi%2BkRqQ%2BzAnfpqIf5t6avQvb3orzx0G7OEVl8Alm5wpgCl2cDA7GlbwE6vDM1tI8BN%2Fp6UexUvmV%2FzQapEEMymhl4oYKR%2Bn1zLziB1j1ZuAXhm%2Bp59NsSfkhwOhntiALT64Xb89zr%2FXNnTVu3Jaem7jcF%2BVqbWNHY4y3kQBqTgdkuh01P%2BOj17E0OakNB6nT4Q%3D>



Age: 23 Gender: Female
Clinical Information: CIN smear 3 years ago.

Decidualisation of cervical stroma

<https://www.virtualpathology.leeds.ac.uk/slides/library/view.php?path=%2FResearch%2FSlide%20Library%2FR%20Bishop%20Collection%2FCard%20index%2FSet%2FGynaec%2F33662.svs>



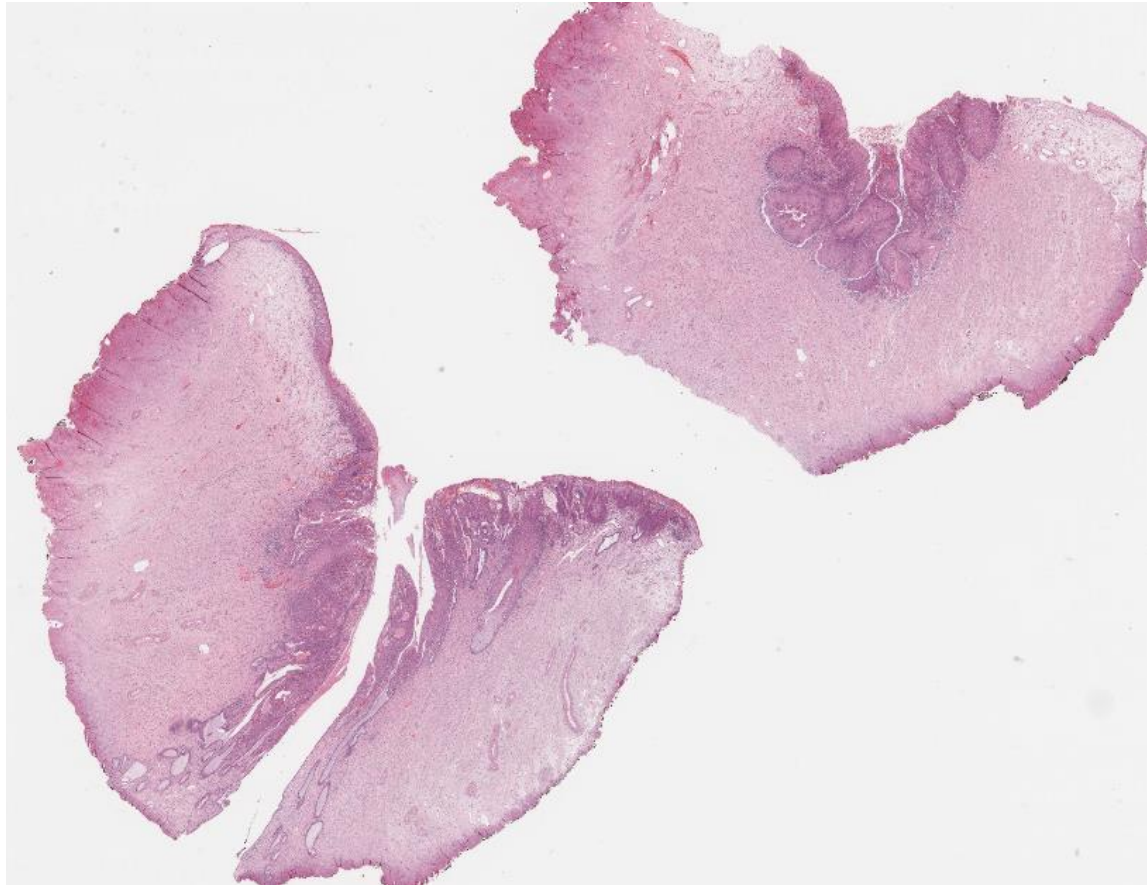
Diagnosis?

SCC-HPVA (if p16 positive)

Squamotransitional carcinoma pattern

- Multilayered epithelium with variable degree of squamous &/or transitional cell differentiation covering true papillae with fibrovascular cores
 - Relatively low nuclear:cytoplasmic ratio
 - Hyperchromatic nuclei
 - Nucleoli may be evident
 - Occasional keratinization &/or keratin pearls may be present

<https://www.virtualpathology.leeds.ac.uk/slides/library/view.php?path=%2FResearch%204%2FSlide%20Library%2FMISCELLANEOUS%2FACCP%2FMAY2007%2F38540.svs>



Diagnosis?

SCC-HPVA (if p16 positive)

Microinvasive pattern

IA1 Measured stromal invasion <3 mm in depth

Multiple foci? Measure the deepest. Is it 2 tumours – use common sense; is it at least 5 mm apart?

HPV-independent SCC

- True cervical cancers that are independent of high-risk HPV, “a confirmed HPV-independent cervical squamous cell carcinoma has not yet been reported” Xing, 2021
- Lost HPV expression,
- SCC due to low-risk HPV (1%)
- False-negative results.

<https://www.frontiersin.org/articles/10.3389/fonc.2020.606335/full>