Mogucnosti kolposkopije u dijagnosticiranju mikroinvazivnog raka vrata maternice

Dubravko Barišić

Što je mikroinvazivni rak vrata maternice (MIC)?

- Mikrokarcinom *(Mestwerdt 1947.)*
- Rana stromalna invazija
- Superficially invasive carcinoma of the cervix *(Gershenson D. i sur.Gynecologic Cancer: Controversies in Management, Elsevier Churchil Livingstone, 2004.)*

FIGO klasifikacija

Table 10–1. FIGO Staging of Early Cervical Cancer: Stage Ia-1b

Stage Ia	Invasive carcinoma that can be diagnosed only by microscopy. All macroscopically visible lesions—even those with superficial invasion—are allotted to stage 1b. Invasion is limited to a measured stromal invasion, with a maximal depth of 5.0 mm and a horizontal extension of not >7.0 mm. Depth of invasion should not be >5.0 mm taken from the base of the epithelium of the original tissue, superficial or glandular. The involvement of vascular spaces—venous or lymphatic—should not change the stage allotment.
Ia1	Measured stromal invasion of not >3.0 mm in depth and extension not >7.0 mm
Ia2	Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7 mm
Stage Ib	Cancers with a depth of more than 5 mm and/or with a length of more than 7 mm are allocated to stage Ib. The presence (or absence) of capillary-like space involvement should be noted but does not influence stage Ia.

From International Federation of Gynecology and Obstetrics: Staging announcement. FIGO staging of gynecological cancers: Cervical and vulva. Int J Gynecol Cancer 1995;5:319.

"Mikroinvazivna lezija je ona u kojoj neoplastični epitel invadira stromu na jednom ili više mjesta do dubine od 3 mm ili manje ispod bazalne membrane, i pri kojoj nema invazije limfnih i kapilarnih prostora"

Komitet za nomenklaturu Society of Gynecologic Oncologists - SGO

Radi se o malim lezijama koje imaju dobru prognozu pa se mogu liječiti konzervativnijim pristupom

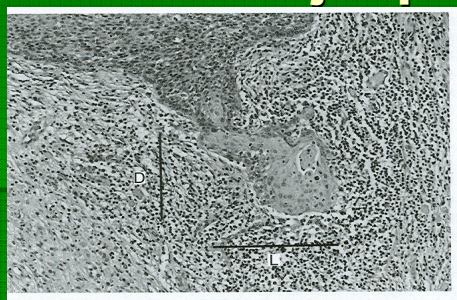
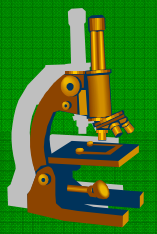
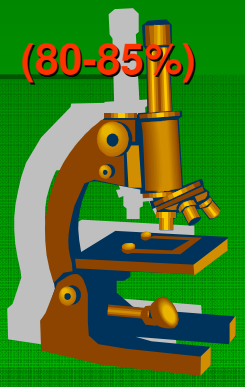


Figure 10–2. Superficially invasive squamous cell carcinoma (early stromal invasion)—FIGO stage Ia1. A tongue of neoplastic cells with cytoplasmic differentiation extends from the base of the surface epithelium, which displays features of high-grade squamous intraepithelial lesions. The depth of invasion (D) is measured from the site of origin of the invasive focus. The horizontal spread (L) is measured across the focus parallel to the surface. If more than one of these foci (i.e., spray pattern) is present, a summation is made of each focus, ignoring intervening stroma. In this case, the depth is 0.2 mm, and the length is 0.25 mm (hematoxylin & eosin, magnification × 200).



histološki

- **planocelularni ili skvamozni (80-85%)**
- adenokarcinom (15%)
- adenoskvamozni (3-5%)
- ostali



problemi

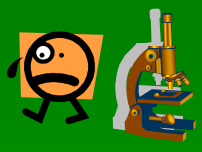
- uglavnom bez subjektivnih tegoba
- nema klinički vidljive lezije (ako postoji, to je po definiciji Ib1)
- pouzdanost citologije 36-87%*
- citologija lažno negativna (44% od 143 MIC sa negativnim cit. nalazom**)

*Ng AB, Reagan JW, Lindner EA. Acta Cytol 1972;16:5-13

*Rome RM, Chanen W, Ostor AG. Gynecol Oncol1985;22:302-312.

**Rylander E.Acta Obstet Scand 1976;55:361-6.

problemi



- dijagnoza isključivo patohistološkom analizom *(punch ili LLETZ biopsije, ili klinastog isječka tkiva ili konusa)*
- 37,5% mikroinvazija odbačeno zbog nepostojanja jasnog dokaza invazije*
- u 6,8% mikroinvazivnih karcinoma se zapravo radilo o Ib1*

*Sedlis A, Sol S, Tsukada Y, et al. Am J Obstet Gynecol1979;133:64-74.

problemi

- MIC moguć uz HGSIL u citološkom nalazu
- Često CIN 3 na punch biopsiji a na konizatu MIC

problemi

Prognoza je uglavnom dobra, ali…

Table 10–5. Reports of Stage Ia Squamous Cell Carcinoma of the Cervix Treated by Cone Biopsy Alone

Study	Stage	Patients	Recurrence		Term Pregnancies	Follow-up (Mean) (years)
			CIN	Invasion		
Kolstad[85] (1989)*	Ia1 Ia2	41	0	4‖	NS	3-17
Burghardt et al.[89] (1991)*	Ia1	93	NS	1¶	NS	NS
	Ia2	18	NS	3**	NS	NS
Morris et al.[114] (1993)*	Ia1 LVSI–	14	1	0	3	0.1-14 (2.2)
Andersen et al.[115] (1993)†	Ia1 LVSI–	31	1	0	NS	NS (3.0)
Östör & Rome[55] (1994)*	Ia1 Ia2	23	0	1††	NS	0-15
Tseng et al.[116] (1997)‡	Ia1 LVSI–	12	1	0	4	6.7
Andersen et al.[117] (1998)†	Ia1 LVSI–	41	1§	0	6	5-12 (6.8)

*Cold-knife cone.
†Combination laser conization.
‡Loop electroexcisional procedure (LEEP).
§Adenocarcinoma in situ.
‖All were local recurrences.
¶Recurrent cervical cancer 12 years after cone biopsy with negative margins.
**Recurrences at 1, 1, and 3 years after cone biopsy; margins were not stated; and one tumor was a clear cell carcinoma cancer.
††Residual cervical cancer manifested 7 years after cone biopsy with an involved apical margin.
LVSI–, no lymphovascular space involvement; NS, not stated.

Table 10–2. Lymph Node Involvement, Recurrences, and Deaths in Patients with Squamous Cell Carcinomas and Stromal Invasion of 3 to 5 mm

Study*	No. of Cases	Lymph Node Positive	Recurrent Cancer	Died of Disease
Roche et al.[29] (1975)	21	0/21	Not stated (NS)	NS
Leman et al.[76] (1976)	7	0/7	NS	NS
Iversen et al.[77] (1979)	28	NS	2	1
Sedlis et al.[4] (1979)	21	NS	2	2
Hasumi et al.[78] (1980)	29	4/29	NS	NS
Van Nagell et al.[79] (1983)	32	3/32	3	2
Brémond et al.[80] (1985)	26	0/26	0	0
Creasman et al.[81] (1985)	21	0/NS	1	1
Simon et al.[82] (1986)	26	1/NS	0	0
Maiman et al.[83] (1988)	30	4/30	0	0
Ebeling et al.[84] (1989)	62	NS	3	NS
Kolstad[85] (1989)	187	1/NS	8	3
Schumacher et al.[86] (1989)	16	1/NS	2	1
Tsukamoto et al.[87] (1989)	15	0/NS	1	0
Greer et al.[88] (1990)	5	0/NS	0	0
Burghardt et al.[89] (1991)	16	0/NS	2	2
Chakalova et al.[90] (1991)	10	NS	0	0
Copeland et al.[6] (1992)	59	1/29	2	1
Sevin et al.[91] (1992)	36	2/36	4	4
Jones et al.[92] (1993)	24	0/18	1	0
Östör et al.[55] (1993)	31	0/21	1	1
Buckley et al.[93] (1996)	94	7/94	5	4
Creasman et al.[94] (1998)	188	0/51	0	0
Takeshima et al.[30] (1999)	85	5/73	3	3
Total	**1069**	**26/467** (5.6%)	**38/1012** (3.8%)	**25/950** (2.6%)

*In many of these series, the extent of horizontal spread was not stated. Some may have been FIGO stage Ib1 cancers with spread of more than 7 mm. Some nonsquamous tumors may have been included in some series.

Table 10–3. Lymphovascular Space Involvement, Lymph Node Metastases, and Recurrence in Tumors with 3 mm or Less Stromal Invasion

LVSI	Pelvic Lymph Node Metastases	Recurrence
Present	4/86 (4.7%)*	6/131 (4.6%)†
Absent	4/757 (0.5%)	10/1556 (0.6%)

*$P = .01$; risk ratio = 9.18; 95% CI: 1.89-44.61. *P* value for the difference between lymphovascular space involvement (LVSI) positive and negative status was computed using Fisher's exact test. Data from References 6, 29, 30, 55, 76, 78, 79, 81-83, 91, 99, 100, 101.
†$P = .0025$; risk ratio = 7.42; 95% CI: 2.36-22.61. *P* value for the difference between LVSI positive and negative status was computed using Fisher's exact test. Data from References 4, 6, 30, 55, 79, 81-83, 89, 91, 100, 101.

Table 10–4. Lymphovascular Space Involvement, Lymph Node Metastases, and Recurrence in Tumors with more than 3 to 5 mm Stromal Invasion

LVSI	Pelvic Lymph Node Metastases	Recurrence
Present	13/117 (11.1%)*	16/92 (17.4%)†
Absent	10/295 (3.4%)	3/320 (0.9%)

*$P = .006$; risk ratio = 8.07; 95% CI: 1.41-9.07. *P* value for the difference between lymphovascular space involvement (LVSI) positive and negative status was computed using Fisher's exact test. Data from References 6, 29, 30, 55, 76, 78, 79, 81-83, 91, 93, 94.
†$P < 10^{-8}$; risk ratio = 22.25; 95% CI: 5.90-57.96. *P* value for the difference between LVSI positive and negative status was computed using Fisher's exact test. Data from References 4, 6, 30, 55, 79, 81-83, 89, 91, 93, 94.

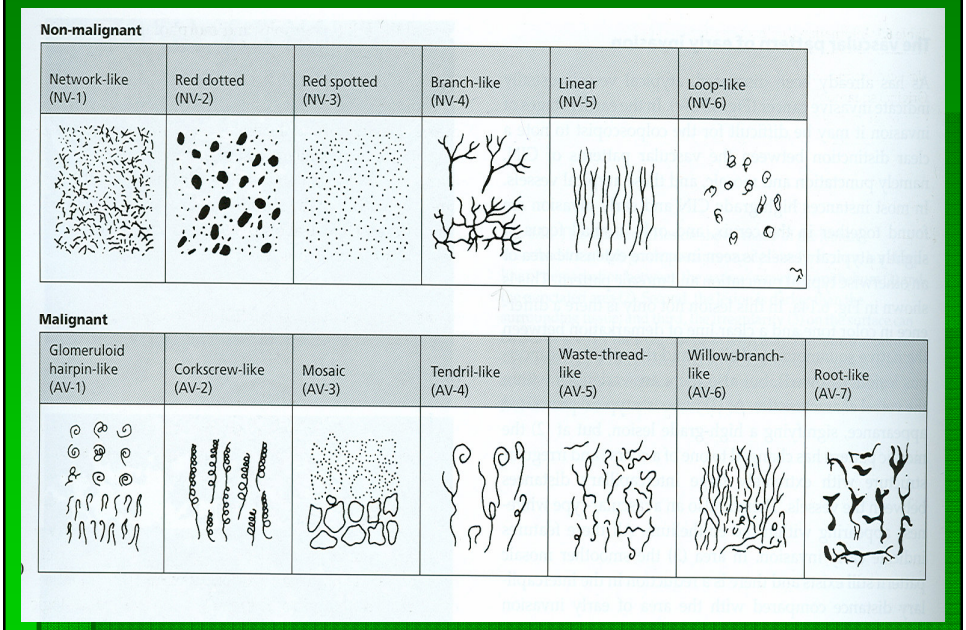
Što može kolposkopija?

Ima li karakteristične kolposkopske slike za MIC?

- Vaskularni crtež je atipičan
- Nema pravilne punktacije i mozaika kao kod HGSILa
- Međukapilarni razmak je različit, uglavnom širok
- Nepravilna zona transformacije je u 42-85% slučajeva povučena u cervikalni kanal*
- Dakle, relativno velik postotak nezadovoljavajućih kolposkopskih nalaza (žene s MIC-om su starije od žena s HGSIL-om)
- Velike zone bez vaskularnog crteža
- Moguće su zone erozije i nekroze sluznice

**Rome RM, Chanen W, Ostor AG. Gynecol Oncol1985;22:302-312.*
**Benedet JL, Anderson GH, Boyes DA. Obstet Gynecol 1985;65:557-62.*

Vaskularni crtež - tipovi



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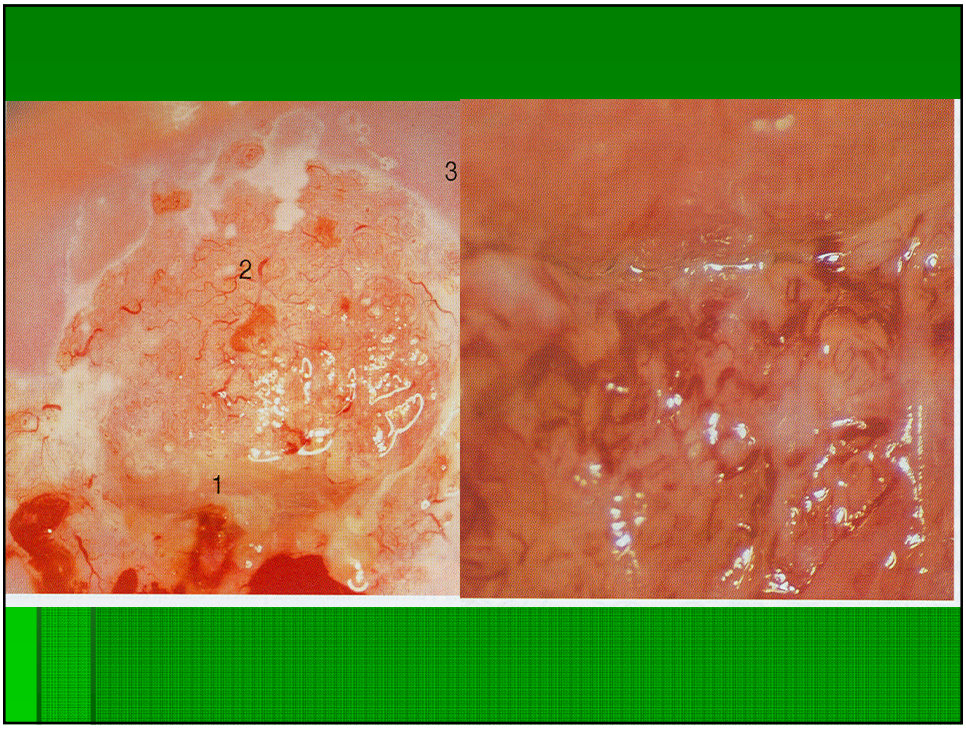

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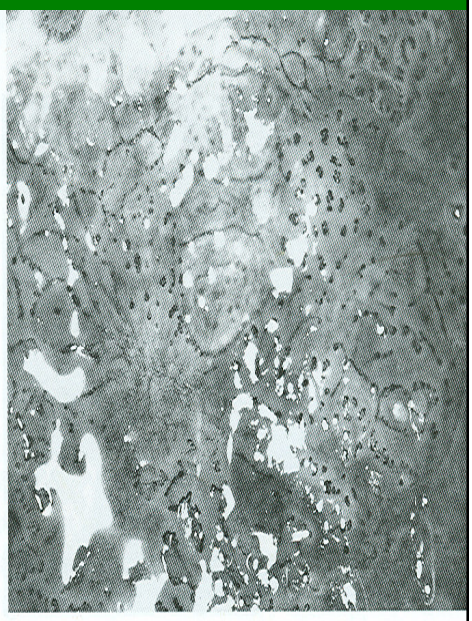
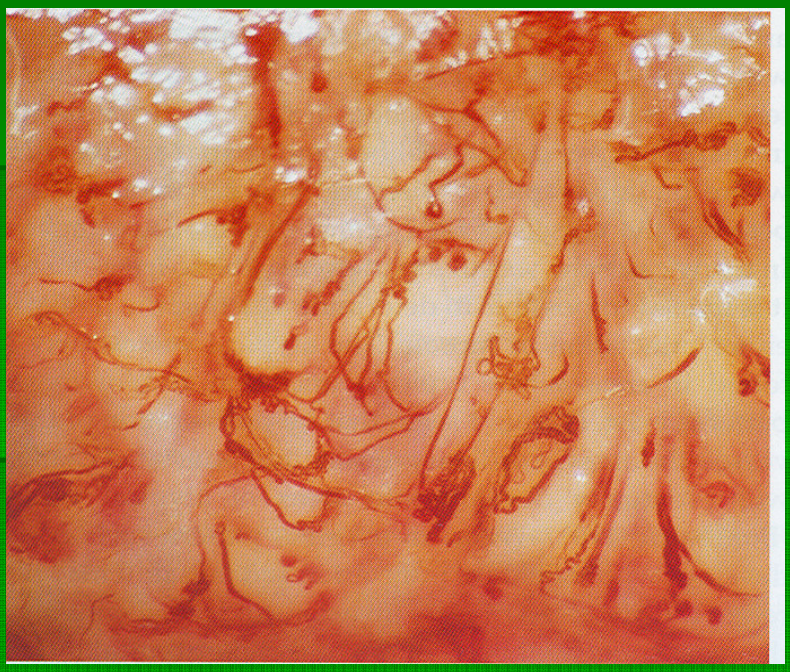


Wide intercapillary distances exist between the hairpinlike
ed vessels and there is a large basketlike dilated vessel in the
dopting a classic mosaic pattern. The underlying lesion is a
intraepithelial neoplasia (CIN) 3.



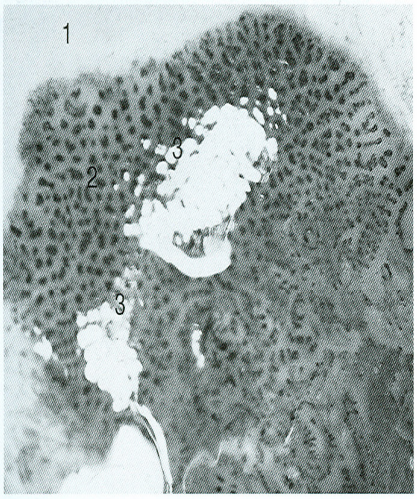
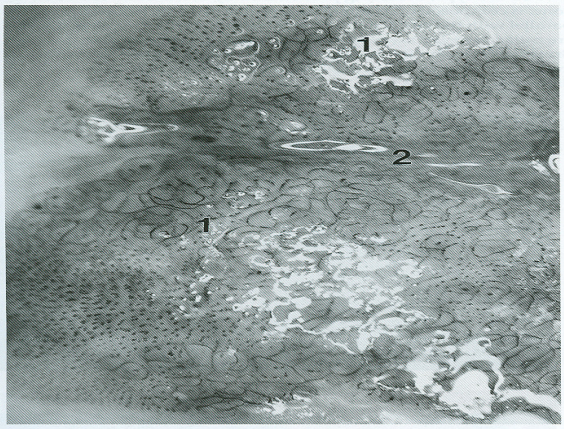
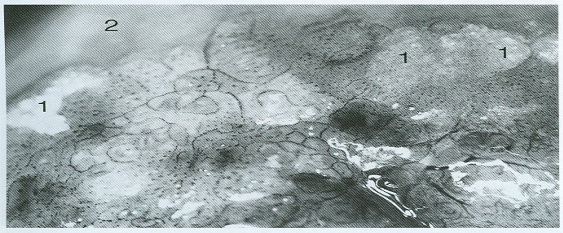


Fig. 6.12 This small focal lesion shows many of the features described for a high-grade precancerous lesion. First, there is a sharp line of demarkation between the native squamous epithelium (1) and the punctated area (2). Second, the lesion is darker than the surrounding tissue; and third, the irregularity (3) on the surface can be clearly seen by the irregular flash reflection. The fourth abnormal sign is that of the hairpinlike and atypical punctated vessels that are coarse; in some places these terminal vessels extend into small papillomatous excrescences (papillary punctation).



. 6.13(a)



. 6.13(b)

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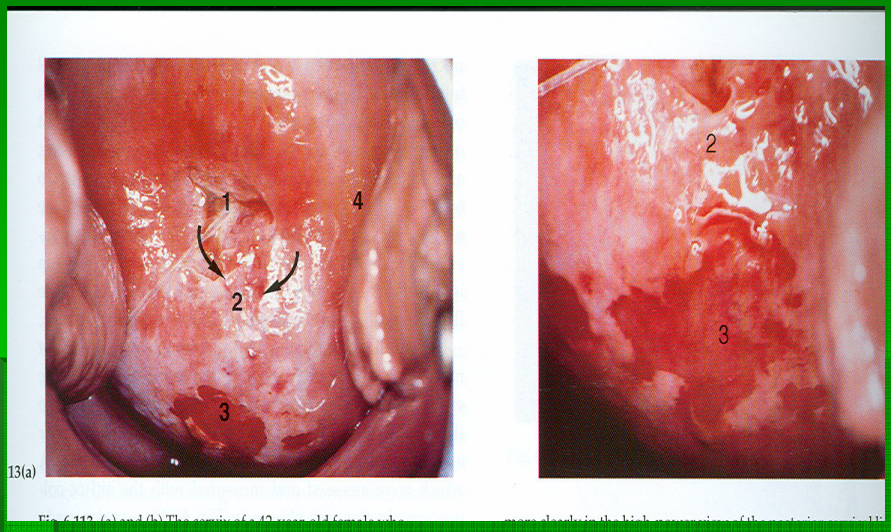

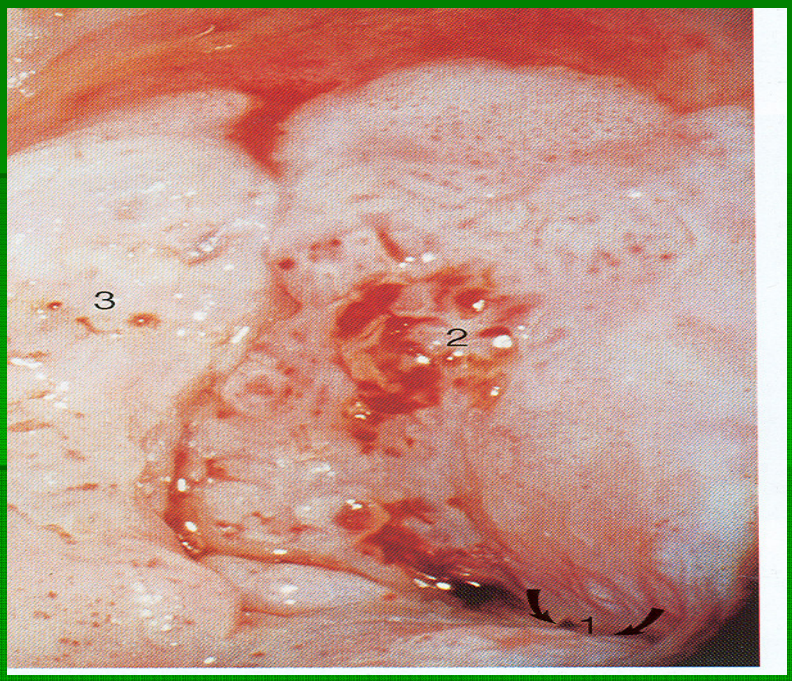

Što može kolposkopija?

Rome RM, Chanen W, Ostor AG. Gynecol Oncol1985;22:302-312.

- Točno 16/55 slučajeva Ia1(29%)
- Točno 36/72 slučaja s prodorom od 1-7 mm (50%)
-

Što može kolposkopija?

Murdoch JB, Grimshaw RN, Morgan PR, et al. Int J Gynecol Cancer 1992;2:129-33.

- "Kolposkopija je pouzdanija ukoliko je invazija dublja od 1 mm"

Što može kolposkopija?

Kennedy AW, et al. Int J Gynecol Cancer 1995;5:117-20.

- "Kolposkopski neprepoznat invazivni rak nađen je u 0.4% do 3% ekscizijskih biopsija učinjenih zbog CINa (najčešće LLETZom)

Što može kolposkopija?

- Omogućava ciljanu biopsiju sa suspektnog područja
- Ukoliko biopsija pokaže invaziju, ili postavi sumnju na mikroinvaziju, obično je neophodna ekscizijska biopsija