

## Histological results after large loop excision of the transformation zone procedure: analysis and frequency distribution

### *Wyniki badań histologicznych po zabiegach szerokiego wycięcia strefy przekształceń nabłonkowych pętlą elektryczną: analiza i rozkład częstości występowania*

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Medical Studies/Studia Medyczne 2022; 38 (2): 109–114

DOI: <https://doi.org/10.5114/ms.2022.117624>

**Key words:** large loop excision of the transformation zone, high-grade squamous intraepithelial lesion, intra-glandular involvement, resection lines, histological results.

**Słowa kluczowe:** zabieg szerokiego wycięcia strefy przekształceń nabłonkowych pętlą elektryczną, płaskonabłonkowa zmiana śródnabłonkowa o wysokim stopniu zaawansowania, zajęcie gruczołów, linie resekcji, wyniki badania histologicznego.

#### Abstract

**Introduction:** The treatment of precancerous changes in the cervix is the base of secondary prevention of cervical cancer and is a part of most national programs for the prevention of the disease.

**Aim of the research:** To perform a frequency analysis of histological results after large loop excision of the transformation zone (LLETZ) for cervical precancerous lesions in an outpatient setting.

**Material and methods:** From 1 January 2017 to 31 July 2021, 189 patients underwent Medical Centre "Prof. Kornovski". The methodology includes the indications for performing the LLETZ procedure, a description of the procedure, the tools and technical parameters, the operation technique, and the histological examination.

**Results:** We present a histological analysis of the preparations after LLETZ, the frequency of glandular involvement in the pathological process, the incidence of thermal damage of the resection lines after the procedure, and the incidence of involvement of carcinoma or high-grade squamous intraepithelial lesion of resection lines after LLETZ.

**Conclusions:** The LLETZ procedure can be diagnostic for the detection of invasive carcinoma in menopausal women, clinically and colposcopically suspected of invasion, but with negative histology from the targeted biopsy. Intra-glandular spread is a sign of high-grade dysplasia and cervical carcinoma in situ. Thermal damage to resection lines is a consequence of LLETZ. These lesions do not compromise the assessment of the resection lines. This shows the possibilities of applying the LLETZ procedure for diagnosing and treating cervical pathologies.

#### Streszczenie

**Wprowadzenie:** Leczenie stanów przedrakowych szyjki macicy stanowi podstawę wtórnej profilaktyki raka szyjki macicy i jest elementem większości krajowych programów zapobiegania tej chorobie.

**Cel pracy:** Przeprowadzenie analizy częstości występowania poszczególnych wyników histologicznych po zabiegach szerokiego wycięcia strefy przekształceń nabłonkowych pętlą elektryczną (LLETZ) wykonanych u pacjentek ze zmianami przedrakowymi szyjki macicy w warunkach ambulatoryjnych.

**Materiał i metody:** Od 1 stycznia 2017 do 31 lipca 2021 roku w Centrum Medycznym im. Prof. Kornovskiego zabiegi LLETZ przeprowadzono u 189 pacjentek. W metodologii badania uwzględniono wskazania do wykonania LLETZ, opis zabiegu, narzędzia i parametry techniczne, technikę operacyjną oraz badanie histologiczne.

**Wyniki:** W pracy przedstawiono wyniki badań histologicznych preparatów przygotowanych po zabiegu LLETZ, a także częstość zajęcia gruczołów w procesie patologicznym, termicznego uszkodzenia linii resekcji po zabiegu oraz występowania raka lub płaskonabłonkowej zmiany śródnabłonkowej o wysokim stopniu zaawansowania w liniach resekcji po LLETZ.

**Wnioski:** Zabieg LLETZ może być wykonywany w celach diagnostycznych w wykrywaniu raka inwazyjnego u kobiet w okresie menopauzy, u których na podstawie obrazu klinicznego i wyników kolposkopii podejrzewa się zmianę inwazyj-

na, ale wynik badania histopatologicznego po wykonaniu biopsji celowanej jest ujemny. Rozsiew do gruczołów jest oznaką dysplazji wysokiego stopnia i raka szyjki macicy *in situ*. Skutkiem LLETZ jest uszkodzenie termiczne linii resekcji. Zmiany te nie wpływają jednak na ocenę linii resekcji. Uzyskane wyniki wskazują na możliwość stosowania zabiegu LLETZ w diagnostyce i leczeniu patologii szyjki macicy.

## Introduction

The treatment of precancerous changes in the cervix is the basis of secondary prevention of cervical cancer and is part of most national programs for prevention of the disease. It includes destructive and excisional techniques. The indications for treatment are determined by the degree of development of precancerous lesions and the degree of penetration of the atypical area (lesion) into the cervical canal. Excisional techniques are recommended for high-grade precancerous lesions, a completely invisible lesion, or its spread into the cervical canal [1]. The large loop excision of transformation zone (LLETZ) procedure is one of the most commonly used techniques. The histological results of LLETZ are grounds for its adoption as a diagnostic and therapeutic interventional technique for a large part of cervical pathology and a starting point for the follow-up of patients.

## Aim of the research

To analyse the frequency distribution of histological results after LLETZ in an outpatient setting.

## Material and methods

From 1 January 2017, to 31 July 2021, 189 patients underwent large loop excision of the transformation zone (LLETZ) at the Medical Centre “Prof. Kornovski”.

Indications for performing the procedure [1]:

1. The lesion penetrates the cervical canal, and colposcopy or biopsy evaluation is not possible (unsatisfactory colposcopy).
2. Cytology presents repeated suspicion of invasion without colposcopic data for such.
3. Suspicion of an invasive lesion by colposcopy, cytology, or biopsy.
4. Abnormal glandular lesion confirmed by cytology or colposcopy.
5. Cytology presents a more serious finding than colposcopy or forceps biopsy.

### Description of the procedure (equipment and tools)

The anaesthesia is local, using 10 ml of 2% lidocaine solution. Multiple punctures (closer and farther from the cervical canal, deeper and shallower) are made with a 1 ml insulin syringe; the cervicovaginal branches are avoided (at 3 and 9 o'clock) due to the risk of vegetative reactions such as noise in the ears and dizziness. A mandatory scarification test with lidocaine is performed prior to anaesthesia. RR, heart

rate, and saturation are monitored. The operation begins with disinfection of the vagina with Braunol, colposcopy with acetic acid (5%), or Lugol's solution and loop choice. A SURTRON 120 electrosurgical device, SURTRON 120 (cutting mode 100 W and coagulation-60 W – SOFT 100 W 60 W), a smoke evacuation device, and cutting loops were used (Figure 1).

The procedure begins with cutting from left to right and simultaneous powerful aspiration of the smoke from the altered area outlined with Lugol's solution (Figure 2).

Coagulation is included simultaneously with the cutting mode. In large lesions of the exocervix, the lesion's periphery is additionally cut to a clean cut with a smaller loop. In lesions spreading to the cervical canal, the top of the resection surface is additionally excised with a special smaller and thinner loop. After the operation, the resection surface is coagulated with a spherical electrode.

Finally, the wound surface is smeared with sterile Monsel's solution after disinfection with Braunol. The view of the specimen is given in Figure 3).

## Histological examination

The histological specimens of all patients were examined by only one experienced and highly qualified pathologist. The histological preparation, the resection lines (of the exocervix, endocervix, and the cone tip), as well as the cervical gland involvement, were examined. The thermocoagulation changes of the resection lines, if any, were reported.

## Results

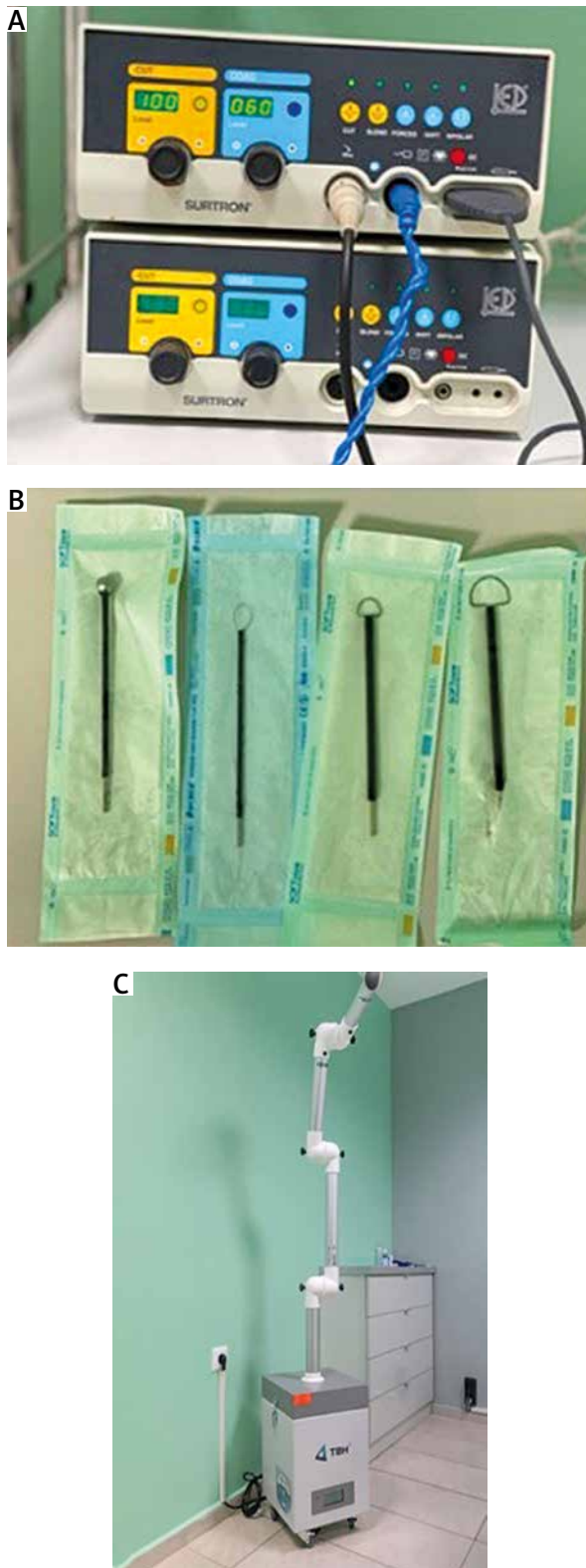
The distribution of patients by age, and parous and menopausal status is presented in Table 1.

Results required from the pathological examination:

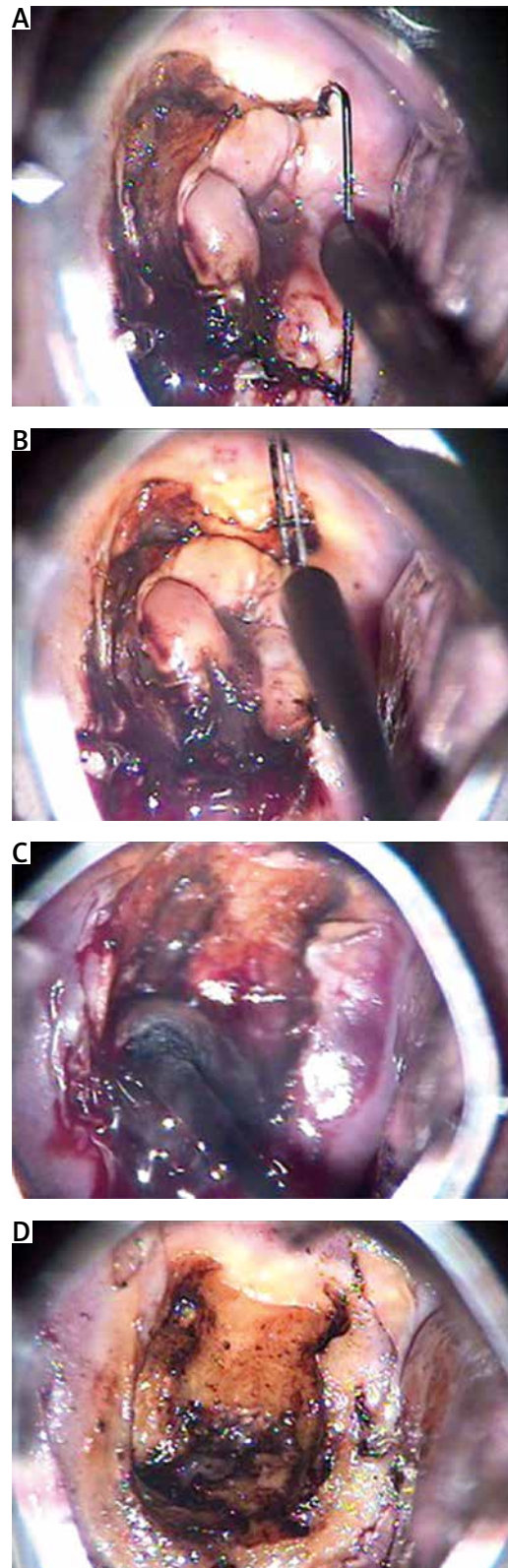
1. Results of the histological analysis of the preparations after LLETZ;
2. Frequency of glandular involvement by the pathological process;
3. Frequency of thermal damage to the resection lines after LLETZ;
4. Incidence of involvement of carcinoma and high-grade squamous lesion (HSIL) resection lines after LLETZ.

The results of the histological analysis of the preparations after LLETZ are presented in Table 2.

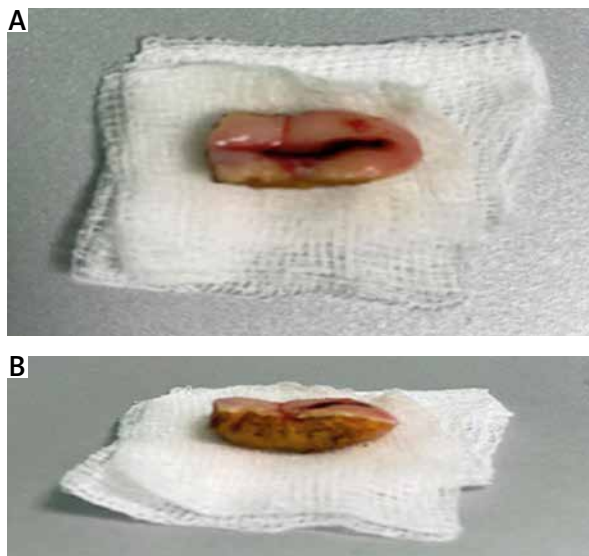
Low-grade squamous lesion (LSIL) was diagnosed in nearly 1/3 of LLETZ cases. The reason for this is the indications for applying excision techniques. The atyp-



**Figure 1.** The equipment used: **A** – electro-surgical apparatus SURTRON 120; **B** – types of cutting loops and spherical coagulation electrode; **C** – powerful smoke evacuation apparatus



**Figure 2.** The procedure itself: **A** – the beginning of the procedure; **B** – the end of the procedure; **C** – coagulation with a ball electrode; **D** – the cervix after the procedure



**Figure 3.** The postoperative specimen: **A** – postoperative (removed) preparation – in full-face; **B** – postoperative (removed) preparation – in profile

**Table 2.** Distribution of patients according to the histological results after LLETZ

Distribution	N (%)
LSIL	60 (31.7)
HSIL	108 (57.1)
Cervical cancer in situ	11 (5.8)
AIS	3 (1.6)
Microinvasive cervical cancer	4 (2.1)
Invasive cervical cancer	3 (1.6)

LSIL – low-grade squamous lesion, HSIL – high-grade squamous lesion, AIS – adenocarcinoma in situ.

**Table 4.** Frequency of thermal damage to the resection lines after LLETZ

Thermal damage to the resection lines (exocervix, endocervix, cone tip), no dysplasia present	15 (7.9%)
Ectocervix	15 (7.9%)
Endocervix	15 (7.9%)
Cone tip	15 (7.9%)

ical area spread into the cervical canal without colposcopy tracing of the boundaries of the atypical area is an indication for LLETZ [1]. In all cases of LSIL spread to the cervical canal, an LLETZ procedure was performed. Before loop excision, the diagnosis was made by colposcopy, biopsy, and cytology. Cervical cancer in situ, adenocarcinoma in situ (AIS), and microinvasive cervical cancer were found in 17 patients, showing the role of loop excision in diagnosing and treating these diseases. In cases of clinical suspicion of invasive can-

**Table 1.** Patients' characteristics

Patients' characteristics	N	%
Total	189	100.0
Age groups:		
20–30	37	19.5
31–40	91	48.2
41–50	50	26.5
51–65	11	5.8
Parous status:		
Parous	144	76.2
Non-parous	45	23.8
Menopausal status:		
Perimenopause	177	93.7
Postmenopause	2	6.3

**Table 3.** Frequency of cervical glandular involvement

Cervical glandular involvement	64 (33.9%)
LSIL	2/64 (3.1%)
HSIL	45/64 (70.3%)
Cervical cancer in situ	7/64 (10.9%)
AIS	3/64 (4.7%)
Microinvasive cervical cancer	4/64 (6.3%)
Invasive cervical cancer	3/64 (4.7%)

LSIL – low-grade squamous lesion, HSIL – high-grade squamous lesion, AIS – adenocarcinoma in situ.

cer or inconclusive data from pinch biopsy, the LLETZ procedure is recommended for diagnostic purposes in postmenopausal women with atrophic changes in the cervix to exclude or confirm invasive cancer.

The frequency of glandular involvement in the pathological process is presented in Table 3.

Of the total number of cases with intra-glandular involvement, the highest share falls on those with HSIL (70.3%), because the greater number of patients (108/189) have this diagnosis. On the other hand, glandular involvement in the pathological process can be considered a sign of the severity of the disease. The more severe the disease, the higher the incidence of cervical glandular involvement: in LSIL patients, the incidence is 2/60 (3.3%); in those with HSIL – 45/108 (41.7%); in cervical cancer in situ – 7/11 (63.6%); in AIS – 3/3 (100%); in microinvasive cervical cancer – 4/4 (100%); in invasive cervical cancer – 3/3 (100%). Thus, this histological indicator can be interpreted as a predictive factor — the involvement of the cervical glands is associated with the severity of the process.

The frequency of thermal damage to the resection lines after LLETZ is presented in Table 4.

**Table 5.** Incidence of involvement of carcinoma and HSIL resection lines after LLETZ

Involvement of resection lines	HSIL n (%)	Cervical cancer n (%)
Involvement of ectocervix, endocervix, and cone tip	2 (1.05)	3 (14.25)
Endocervical involvement	3 (1.6)	1 (4.75)
Cone tip involvement	2 (1.05)	0
Total	7 (3.7)	4 (19)

Thermocoagulation changes in the resection lines after electroconvulsive excision may complicate the pathologist's histological evaluation and are pointed out as one of the disadvantages of this excision method. The degree of thermal damage depends on the generator of electricity, the strength of the electric current, the mode of cutting, the time of passage of the loop through the fabric and the material, and the thickness of the loop. The pathologist's experience in these cases is crucial to assess and evaluate the status of the resection lines and the presence of dysplasia, despite the thermocoagulation damage to the tissue.

We found thermal damage without dysplasia in 7.9% in the present study. Therefore, thermal changes in the resection lines are not an obstacle to adequate histological examination. This damage is due to the loops' characteristics (thickness and strength) and the mode of simultaneous cutting and coagulation of the generator. This approach ensures a bloodless operation, although it takes longer and leads to these thermocoagulation changes in the cone.

#### Incidence of involvement of carcinoma and HSIL resection lines after LLETZ

Twenty-one patients were diagnosed with cervical cancer after the LLETZ procedure: cervical cancer in situ – 11; AIS – 3; microinvasive cervical cancer – 4; and invasive cervical cancer – 3. Involvement of the resection lines was established in 4 cases — 3 with invasive carcinoma and 1 with microinvasive. In cases of invasive cancer, the LLETZ procedure was performed for diagnostic purposes. This is required for postmenopausal women in whom atrophy does not allow colposcopy, histological examination, or cytology to diagnose definitively, despite the suspicion of invasion. On the other hand, the resection lines are tumour free in patients diagnosed with cervical cancer in situ, including adenocarcinoma, and the other 3 with microinvasive carcinoma.

It is interesting to note the histological type and degree of dysplasia in the seven cases of HSIL resection line involvement: microinvasive carcinoma – 1; AIS – 1; cervical cancer in situ – 2; and HSIL – 3. Therefore, in AIS, the resection lines are affected in 33% (1/3) of the cases; in cervical cancer in situ – 18.2% (2/11); in HSIL – 2.8% (3/108); and in Ca microinvasive – 25% (1/4). These results indicate that the LLETZ procedure

can be curative in high-grade squamous cell carcinoma lesions and in most cases of squamous cell carcinoma in situ. The LLETZ technique described above contributes to these results. The colposcopy before operation and the delineation of the atypical area with Lugol's solution, and hence the choice of adequate loop size, also contribute to the above. In atypical areas on the exocervix that are larger than the loop, an additional incision of residual dysplastic tissue with a smaller loop is required until a clean cut is reached (Table 5).

#### Discussion

The involvement of resection lines by the dysplastic process, especially high-grade dysplasia (HSIL), is the most critical histological indicator after the LLETZ procedure. This indicator is a certificate of radicalism and the therapeutic effect of the procedure. On the other hand, it is the most important prognostic factor for recurrence or progression of the precancerous process. In the current series of patients, we found the frequency of HSIL resection lines to be 3.7% of all LLETZ patients (7 of 189).

Different authors report different frequencies, factors, and localization of positive resection lines. A meta-analysis of 66 studies, with 35,109 women with CIN, found 23% involvement of the resection lines. Postoperative recurrence of HSIL has been demonstrated in 18% of patients with positive resection lines but only in 3% of those with dysplasia-free resection lines [2]. These data support the thesis of the strong prognostic significance of dysplasia-affected resection lines for the recurrence of the disease. Conversely, not all patients (only 18%) with involvement of the resection lines develop a relapse. A study by Chen *et al.* found a 13% incidence of resection line involvement (R+) in 1113 patients (141/1113) diagnosed with CIN3 and treated with LEEP and scalpel conization [3]. The localization of the affected resection lines is as follows: ectocervix – 45%, endocervix – 32%, and ecto-endocervix – 23%. Menopausal women had R(+) in 35.4% and premenopausal women in 11.6% of the cases. The authors identified the factors for the R(+) occurrence: degree of SIL, lesion size, excision technique (LLETZ – 24.1% R+; scalpel conization – 4.8% R+), and loop size in LEEP. Panna *et al.* reported 26.8% R(+) in 463 women undergoing LLETZ and scalpel conization [4]. The affected lines were on the ectocervix – 9%, en-



docervix – 10%, and ecto-endocervix – 7%. According to this study, the factors responsible for R (+) are the skills of the surgeon, the type of excision technique (R+ are found more often after LEEP), the histological diagnosis, and the purpose of conization (diagnostic or therapeutic). There is often no clear colposcopy or biopsy evidence of invasion due to atrophy in postmenopausal women, although it may be suspected. In these cases, LLETZ is recommended for diagnostic purposes to prove or rule out invasive cancer. When carcinoma is diagnosed, resection lines are usually involved in the process. In another study, R (+) was found in 33%, with the ectocervix affected in 8%, the endocervix in 22%, and the ectocervix in 3% of cases [5]. According to the researchers, the prognostic factors for R (+) are age > 35 years, atypical area size, and intra-glandular involvement. Papoutsis *et al.* reported a similar frequency — 30.7% of R (+) with involvement of the ectocervix in 10.4%, endocervix – in 18%, and ecto/endocervix – in 2.3% of cases [6].

The LLETZ procedure has been associated with more frequent involvement of the resection lines than scalpel conization in glandular lesions (adenocarcinoma in situ – AIS) [7, 8]. According to one study, the incidence of R (+) in such lesions after scalpel conization is 35%, while after LLETZ it is 56% [7]. Van Hanege *et al.* published similar results in young patients with AIS: R (+) after LLETZ – 27%, and after scalpel conization – 21%, but the authors did not find a significant difference between the 2 excision techniques, despite scalpel conization being the method of choice for glandular lesions [8].

In the current series of patients, the incidence of R (+) was 33% in AIS, although only in 3 patients, which confirms the thesis that loop excision is unsuitable for adenocarcinoma lesions.

## Conclusions

Histological results of LSIL in postoperative preparation are possible if the indications for performing LLETZ are observed. The LLETZ procedure may be diagnostic for confirming invasive carcinoma in postmenopausal women, clinically and colposcopically suspected of invasion, but with negative histology from the targeted biopsy. Intra-glandular involvement is a sign of high-grade dysplasia and carcinoma colli uteri in situ. The thermal damage to the resection lines is a consequence of LLETZ and is found in 7.9% of the cases in the present study. These damages do not compromise the assessment of the resection lines. The incidence of involvement of the resection lines after LLETZ in patients with HSIL is 2.8%. This is due to the operation technique. Involvement of cone resection lines in patients diagnosed with cervical cancer in situ occurs in 18.2% of cases. This shows the possibilities of using the LLETZ procedure for the diagnosis and treatment of this pathology.

## Conflict of interest

The authors declare no conflict of interest.

## References

1. Prendiville W. Large loop excision of the transformation zone. *Clin Obstet Gynecol* 1995; 38: 622-339.
2. Ghaem-Maghani S, Sagi S, Majeed G, Soutter WP. Incomplete excision of cervical intraepithelial neoplasia and risk of treatment failure: a meta-analysis. *Lancet Oncol* 2007; 8: 985-993.
3. Chen Y, Lu H, Wan X, Lv W, Xie X. Factors associated with positive margins in patients with cervical intraepithelial neoplasia grade 3 and postconization management. *Int J Gynaecol Obstet* 2009; 107: 107-110.
4. Panna S, Luanratanakorn S. Positive margin prevalence and risk factors with cervical specimens obtained from loop electrosurgical excision procedures and cold knife conization. *Asian Pac J Cancer Prev* 2009; 10: 637-640.
5. Shaco-Levy R, Eger G, Dreiherr J, Benharroch D, Meirovitz M. Positive margin status in uterine cervix cone specimens is associated with persistent/recurrent high-grade dysplasia. *Int J Gynecol Pathol* 2014; 33: 83-88.
6. Papoutsis D, Panikkar J, Gornall A, Blundell S. Does the number of tissue fragments removed from the cervix with excisional treatment for CIN pathology affect the completeness of excision and cytology recurrence at follow-up? An observational cohort study. *J Obstet Gynaecol* 2016; 36: 251-256.
7. Costales AB, Milbourne AM, Rhodes HE, Munsell MF, Walbillich JJ, Brown J, Frumovitz M, Ramondetta LM, Schmeler KM. Risk of residual disease and invasive carcinoma in women treated for adenocarcinoma in situ of the cervix. *Gynecol Oncol* 2013; 129: 513-516.
8. Van Hanege N, Barroilhet LM, Nucci MR, Bernstein M, Feldman S. Fertility-sparing treatment in younger women with adenocarcinoma in situ of the cervix. *Gynecol Oncol* 2012; 124: 72-77.

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