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Influence of high risk HPV genotype on colposcopic performance: A large prospective study demonstrates improved detection of disease with ZedScan *I*, particularly in non-HPV 16 patients

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ABSTRACT

Objective: To assess the influence of high-risk Human Papilloma Virus (hrHPV) genotyping on the detection of high-grade disease (CIN2+) using colposcopic impression both with and without electrical impedance spectroscopy (ZedScan *I*) as an adjunct.
Study design: A prospective cohort of women with a known hrHPV genotype referred to a single colposcopy service.
Results: 839 women underwent colposcopy and ZedScan *I* examination. 613 women were referred with abnormal cytology; 411 (67%) with low-grade dyskaryosis (67%) and 202 (33%) with high-grade dyskaryosis. 187 were referred with persistent hrHPV but negative cytology. 35 were attended for follow up and 4 for a clinical indication. 159 (19%) women were positive for HPV16 only; 54 (6%) with HPV18 only, 443 (53%) women were positive for hrHPV other types (HPV O). 183 (22%) were positive for multiple hrHPV genotypes. CIN2+ was present in 170 (84.2%) of high-grade and 69 (16.7%) of low-grade cytology referrals. Colposcopy was better at detecting HPV16 associated CIN2+ than that associated with HPV18 or HPV O (86.9% vs 79.7%, $p = 0.0191$). ZedScan *I* increased the detection of CIN2+ from 85.6% to 96% irrespective of hrHPV genotype status ($p < 0.0001$).
Conclusion: The use of an electrical impedance spectroscopic device (ZedScan *I*) increases detection of CIN2+ irrespective of hrHPV genotype.

Introduction

It is widely accepted that the vast majority of invasive cervical cancers are caused by persistent high-risk Human Papilloma Virus (hrHPV) infections [1,2]. There is also little doubt that well organised cervical screening programmes have significantly reduced rates of cervical cancer by the detection and treatment of high-grade cervical intraepithelial neoplasia (CIN2/3 or HSIL) [3]. Colposcopy and directed biopsy are integral to diagnosing high-grade disease [4] however, colposcopy is highly subjective with a specificity for the detection of high-grade CIN lesions of between 32 and 92% [5]. More recently some studies have demonstrated at least 19–37% of CIN2 or worse is diagnosed on biopsies taken at random from areas of the cervix not identified by acetowhite changes, suggesting not all high-grade lesions may become obvious and small lesions may be easily missed by the colposcopist [4,6,7].

High-risk HPV screening is significantly more sensitive than cytology alone at predicting high-grade disease [8,9]. HPV genotyping; identification of high-risk types (HPV16 and HPV18 in particular) may further improve risk assessment for high-grade disease thus enabling screening programmes to triage women with low-grade cervical cytology to colposcopy or return to routine recall [10,11]. The English Cervical Screening Programme is currently evaluating primary HPV screening at six sites in England [12]. Sheffield is one of these sites.

There is conflicting evidence regarding the role of hrHPV genotype, its effect on colposcopic impression and detection of high-grade disease, with some authors reporting increased detection of abnormalities at colposcopy in the presence of

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HPV16 [13], while others have found no effect on colposcopic impression [14]. As aforementioned the ability of colposcopy to identify high-grade lesions may be dependent on changes to the cervical epithelium after the application of acetic acid and so some high-grade lesions may be missed at colposcopy [15,16]. ZedScan *I* is a handheld CE marked device measuring electrical impedance spectroscopy to differentiate between tissues. The prototype of ZedScan *I* has been shown to improve colposcopic performance by aiding the detection of high-grade CIN independent of the effect of acetic acid on cervical tissue [17]. ZedScan *I* was introduced into routine clinical use in Sheffield in December 2013 to provide the colposcopy team with additional information to support more effective patient management.

This study aims to use one population of women to assess the influence of hrHPV genotyping on the detection of high-grade disease (CIN2+) using colposcopic impression both with and without electrical impedance spectroscopy (ZedScan *I*) as an adjunct.

Materials and methods

A prospective cohort study of women undergoing colposcopy and ZedScan *I* assessment in the Jessop Wing Colposcopy Unit, Sheffield, UK from 1st January 2014 and 31st December 2015 was performed. Five BSCCP accredited colposcopists undertook the examinations. Women who had an adequate colposcopic examination with type 1 and type 2 transformation zones, as per IFCPC terminology, were included in the study, to permit direct comparison between colposcopic impression and EIS readings [18].

All cytology specimens were processed by means of *SurePath*® and the *Roche Cobas 4800* system was used for hrHPV genotyping (this system tests for 14 hrHPV genotypes; 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68). ZedScan *I* colposcopic examinations were carried out according to the manufacturer's protocol. Biopsies and treatments (large loop excision of the transformation zone (LLETZ)) were undertaken based on colposcopic impression and ZedScan *I* results. Random biopsies of normal cervical transformation zone and endocervical curettage were not performed as per local and national guidance [19]. All cervical biopsies and LLETZ specimens were reviewed by specialist gynaecological histopathologists.

Data was collected prospectively on referral indication, hrHPV genotype, final histological diagnosis from direct punch biopsy or LLETZ and entered onto a *Microsoft Excel* ™ database, with Fisher's exact test and Chi squared tests were used to analyse any significant differences between the groups.

The study was performed in the context of a service evaluation and therefore ethical approval was not required.

Results

In total 839 women with a known HPV genotype attended the colposcopy clinic and underwent an adequate colposcopic examination and ZedScan *I* assessment. The mean age of the women referred was 32.9 years (range 20.3–66.1 years). Overall 613 (73%) women were referred with abnormal cytology; 411 with low-grade dyskaryosis (67%) and 202 with high-grade dyskaryosis (33%). A further 187 (22%) were referred with persistent hrHPV but negative cytology (present on two screenings 12 months apart). In addition, there was a small number of women attending for follow up (35), and four who were seen due to a clinical indication. A total of 159 women (19%) were HPV16 positive only; 54 (6%) HPV18 only and 626 women (75%) were positive for hrHPV other (HPV O, comprising of HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) with or without HPV16 or 18 (Fig. 1).

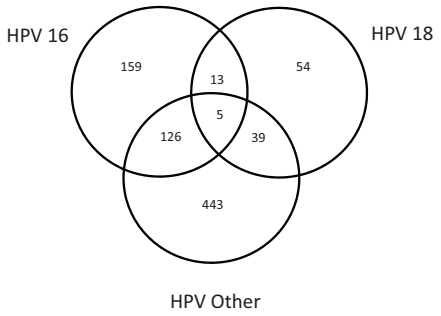

Fig. 1. hrHPV genotype of women referred to the Jessop Wing Colposcopy Unit, Sheffield UK.

Within the cohort of women studied 265 were found to have CIN2+ (31.6%). The incidence of CIN2+ in women referred with high-grade and low-grade cytology was 84.2% (170) and 16.7% (69) respectively (Table 1) and for the women referred with persistent hrHPV positive/cytology negative the incidence of CIN2+ was 9.6% [19]. A further eight cases of high-grade disease were found in the group of women referred with clinical indications and those under follow up for previous CIN.

Women referred with HPV16 genotype

In total 303 women were referred with HPV16, either as a single infection (159), or multiple infections with other hrHPV genotypes (144); 99 (32.7%) had high-grade and 108 (35.6%) low-grade cytology; 82 (27.1%) had negative cytology and 14 were seen for follow up or a clinical indication. Biopsy-proven CIN2+ was identified in 137 (45.2%) women; 92.2% of women referred with high-grade cytology had CIN2+ whereas 28.7% referred with low-grade cytology had CIN2+. The incidence of CIN2+ in women with HPV16 co-infected with HPV18 was 55.6%, and 51.1% in those co-infected with HPV O.

Women referred with HPV18 genotype

A total of 111 women were positive for HPV18 either as a single infection (54) or multiple infections with other hrHPV genotypes (57); 32 (28.8%) were referred with high-grade and 38 (34.2%) with low-grade cytology; 38 (34.2%) had negative cytology and 3 were on follow up or seen for a clinical indication. Biopsy-proven CIN2+ was identified in 35 (31.5%) women; 84.4% of women referred with high-grade cytology had CIN2+ whereas for women with low-grade cytology, 13.2% had CIN2+. The incidence of CIN2+ in those women who also had HPV16 is described above (55.6%) and for those co-infected with HPV O the incidence was 28.2%.

Table 1
High-grade disease detected according to referral cytology and hrHPV genotype status.

	High-grade cytology n = (%)	Low-grade cytology n = (%)
hrHPV ge notype		
HPV 16 only n = 159	42 (89.4%)	12 (23.1%)
HPV 18 only n = 54	10 (83.3%)	1 (6.7%)
HPV O only n = 443	61 (75.3%)	34 (12.7%)
HPV 16 + HPV 18 n = 13	6 (85.7%)	1 (33.3%)
HPV 18 + HPV O n = 39	8 (80.0%)	3 (15.8%)
HPV O ± HPV 16 ± HPV 18 n = 131	43 (95.6%)	18 (34.0%)

Women referred with other hrHPV genotypes (HPV O)

Of the 613 patients with HPV O either as a single infection (433) or multiple infections with HPV16 or 18 (170); 136 (22.2%) were referred with high-grade and 341 (55.6%) with low-grade cytology; 105 (17.1%) had negative cytology with the remainder on follow up or seen for a clinical indication. Biopsy-proven CIN2+ was identified in 181(29.5%) cases; 82.4% of women referred with high-grade cytology had CIN2+ whereas for women with low-grade cytology 16.2% had CIN2+. Excluding women co-infected with HPV16 or 18, only 23.3% had high-grade disease.

hrHPV genotype and detection of high-grade disease by colposcopy and ZedScan I

All 839 women in the service review had a successful assessment with ZedScan *I* as well as a colposcopic examination; 265 had biopsy proven CIN2+. Colposcopy alone detected 221 (83.4%) cases whereas ZedScan *I* detected an additional 34 cases (255 cases in total, 96.2%). The combination of colposcopy and ZedScan detected all cases of CIN2+ (Table 2).

The detection of CIN2+ by colposcopy alone was significantly higher in women with HPV16 than the detection of CIN2+ in women with HPV18 or HPV O; 86.9% *vs* 79.7% ($p = 0.0191$). For all the women, irrespective of their hrHPV genotype status, detection of high-grade disease was higher when ZedScan *I* was used (96.2%) in comparison with colposcopy alone (83.4%) ($p < 0.0001$) (Table 3). ZedScan *I* also increased the detection of CIN2+ in women referred with HPV16 ($p = 0.0171$), and for women referred with HPV18 and or HPV O genotypes ($p < 0.0001$).

Women referred with hrHPV but negative cytology

In total 187 women were seen with persistent hrHPV/negative cytology; 82 (44%) had HPV16 with or without co-infection with other hrHPV subtypes; 34 (18%) had HPV18 with or without co-infection and 71 (38%) had HPV O only. Overall 18 women (9.6%) were found to have CIN2+, three-quarters of whom had HPV16. Colposcopy alone identified 13 of the CIN2+ cases, with ZedScan *I* detecting an additional five cases, a significant increase of 35.5% ($p = 0.045$).

Discussion

With the introduction of HPV testing as part of cervical screening, the potential influence of different hrHPV genotypes, especially HPV16, on colposcopic impression and diagnosis of high-grade CIN may become more significant. HPV16 has the highest oncogenic potential of all hrHPV subtypes [14], with at least 50% of all cases of CIN3 or worse due to HPV16 [20]. Women referred with low-grade cytology who are positive for HPV16 have a higher incidence of high-grade disease compared to those with other hrHPV subtypes [20]. Our study confirms this finding with 28.7% of women with HPV16 and a low-grade cytology having CIN2 + compared to 12.5% who had HPV O; furthermore 14.6% of those with HPV16 and negative cytology had CIN2+ compared to only 5.7% of women with HPV18 or HPV O infections. HPV16 has been shown, in two studies, to result in more definitive visual abnormalities in the cervical epithelium when compared with other types of hrHPV, therefore increasing the likelihood of detection during colposcopic examination relative to other hrHPV types [13,21]. Others however, have reported that the visual appearance of high-grade lesions caused by HPV16 does not differ

Table 2
High-grade disease detected depending on HPV genotype, identified by ZedScan *I* or colposcopy alone.

	Number of women	Total CIN2 or worse detected	CIN2 or worse detected by colposcopic impression alone	CIN2 or worse detected by ZedScan *I*
Total population	839	265 (31.5%)	221 (83.4%)	255 (96.2%)
Women known to have HPV16	303	137 (45.2%)	119 (86.9%)	131 (95.6%)
Women known to have non-HPV16 (HPV 18 and/or O)	536	128 (23.9%)	102 (79.7%)	124 (96.9%)

Table 3
Comparison of detection high-grade disease detected by colposcopy alone vs ZedScan *I*.

	Method of detection	Number of CIN2 or worse detected	Number of CIN2 or worse not detected	Detection rate (95% confidence interval)	Fisher's exact test, two-tailed
All women with known HPV status	**Total**	**265**			
	Colposcopic Impression	221	44	83.4% (78.4–87.4)	$P < 0.0001$
	ZedScan *I*	255	10	96.2% (93.1–98.0)	
HPV 16	**Total**	**137**			
	Colposcopic Impression	119	18	86.9% (80.1–91.6)	$P = 0.0171$
	ZedScan *I*	131	6	95.6% (90.6–98.2)	
HPV 18 and/or O	**Total**	**128**			
	Colposcopic Impression	102	26	79.7% (71.9–85.8)	$P < 0.0001$
	ZedScan *I*	124	4	96.9% (91.9–99.0)	

significantly from those due to other hrHPV subtypes [14]. There is general agreement, that high-grade disease related to HPV16 appears to develop more rapidly and is more commonly found in younger women than disease caused by other hrHPV types, thereby allowing it to be seen earlier and more easily at colposcopy. The mean age of the patients in Jeronimo's [13] paper was much younger than those in Marel's [14] study; 24 vs 36.5 years and this has been suggested as a possible reason for the differences in the findings. The NHS cervical screening programme offers screening to women between the ages of 25 and 65, women under 25 are referred to colposcopy only if they have symptoms or signs of a cervical cancer. Our study population reflects this practice with a mean age at referral of 32.9 years (range 20.3–66.1 years). The proportion of high-grade cytology referrals in the study by Marel et al. [14] was much higher (52.3%) compared to our study (33%) and so it is not surprising the overall prevalence of biopsy-proven high-grade disease was lower in our study compared to Marel et al. [14] (43.6% *vs* 31.6). We also found the prevalence of high-grade disease increased to 45.2% in women with HPV16 with 92.2% of women referred with high-grade cytology and HPV16 having CIN2+. In this study the detection rate of CIN2+ by colposcopy alone was significantly higher if a HPV16 related high-grade lesion was present, 86.9% vs 79.7% ($p = 0.0191$), so concurring with Jeronimo's findings [13,21]. The difference in outcomes for colposcopy based on hrHPV genotype may, in part, be explained by the age and the prevalence of high-grade cytology and high-grade disease in the study population.

Most women referred with abnormal cytology were positive for HPV O but had a lower incidence of CIN2+ (23.3%) when compared to women referred with HPV16 either as a single infection (45.2%) or multiple infections (51.1%–55.6%) with other hrHPV genotypes. The presence of HPV18 did not appear to increase the likelihood of identifying high-grade disease in women referred with abnormal cytology; the incidence of CIN2+ was 84.4% for women with high-grade cytology, almost identical to the overall incidence in this group, and 13.2% for low-grade referrals, again very similar to the overall incidence; 15.4%.

With the increased sensitivity of HPV testing in comparison to cytology alone, many women with high-grade disease are likely to be seen in colposcopy much earlier, before the disease is visible with acetic acid. This highlights the need for an assessment that does not rely on visual inspection of acetowhite changes alone [22]. ZedScan *I* measures electrical impedance spectroscopy across a defined range of current frequencies to differentiate between normal and abnormal cervical cell structures. Alterations in impedance spectra reflect changes in both extra and intra-cellular structure associated with the development of CIN and are not dependent on HPV infection. The influence of hrHPV genotype on the performance of ZedScan *I* has not previously been demonstrated. This study shows how detection rates for high-grade disease remained reassuringly high (96–97%) regardless of which hrHPV genotype was present, indicating that hrHPV has no impact on the performance of the ZedScan *I*.

The introduction of vaccination against HPV16 and 18 is expected to change the epidemiological profile of HPV infection with less HPV16/18 related disease leading to concerns regarding the accuracy of colposcopy in detecting high-grade disease [1]. A consequence of the implementation of primary screening or co-testing with HPV is the referral to colposcopy of women with persistent HPV infection and negative cytology. The prevalence of high-grade disease in this group is low (9.6%) as we have shown. Colposcopy has been shown to perform poorly in patient populations with low prevalence of disease and less visually orientated diagnostic methods may therefore become more necessary in attempting to identify much rarer CIN2+ [7,22,23].

Even if HPV16 is present high-grade disease may be missed at colposcopy [24]. Random biopsies taken at colposcopy have been reported to identify many more cases of high-grade disease (19–37%) that would have been missed if colposcopically directed biopsies only were taken [4,7,25]. In our study a high-grade referral that is also HPV16 positive has a PPV of 91.9% for CIN2+, however three of the 91 women with CIN2+ were identified by ZedScan *I* alone.

The strengths of this study are the large number of women examined by the combination of colposcopy and ZedScan *I* within an organised screening programme following national colposcopy practice guidelines at a large colposcopy clinic. Several trained colposcopists were involved in the evaluation, which was embedded into normal routine practice and hence the results are clinically relevant. The weaknesses are the evaluation was only undertaken in one colposcopy clinic, we did not take random biopsies to exclude or confirm disease status in all women and women with type 3 transformation zones were excluded. The only way to establish the true disease status in any colposcopy study would be to undertake an excisional procedure in all cases, which of course would be unethical.

Conclusion

Women referred with abnormal cytology after primary testing for hrHPV are most likely to be positive for hrHPV O genotypes. Infection with HPV16, either as a single infection or multiple infections with other hrHPV genotypes, is associated with a high incidence of high-grade disease. Colposcopy detects more HPV16 associated high-grade disease when compared with non-HPV16 disease but this may reflect the age and the prevalence of disease in the population studied. The use of an electrical impedance spectroscopic device (ZedScan *I*) increases detection of CIN2+ irrespective of hrHPV genotype.

Disclosure of interests

JAT and BHB hold patents related to the technology. They are shareholders in Zilico Ltd and receive consultancy fees. TJH is a shareholder.

References

[1] Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. Lancet 2007;8(370(9590)):890–907.
[2] Kjær SK, Frederiksen K, Munk C, Iftner T. Long-term absolute risk of cervical intraepithelial neoplasia grade 3 or worse following human papillomavirus infection: role of persistence. J Natl Cancer Inst 2010;6(102(19)):1478–88.
[3] Lynge E. Cohort studies in the evaluation of cervix cancer screening, for the European Network of Cancer Registries. In: Sankila R, Démaret E, Hakama M, Lynge E, Schouten LJ, Parkin DM, editors. In Evaluation and Monitoring of Screening Programmes. . p. 119–32 for the European Network of Cancer Registries.
[4] Jeronimo J, Schiffman M. Colposcopy at a crossroads. Am J Obstet Gynecol 2006;195:349–53.
[5] Stoler MH, Vichnin MD, Ferenczy A, Ferris DG, Perez G, Paavonen J, et al. The accuracy of colposcopic biopsy: analyses from the placebo arm of the Gardasil clinical trials. Int J Cancer 2011;128(6):1354–62.
[6] Pretorius RG, Belinson JL, Burchette RJ, Hu S, Zhang X, Qiao YL. Regardless of skill, performing more biopsies increases the sensitivity of colposcopy. J Low Genit Tract Dis 2011;15(3):180–8.
[7] Wentzensen N, Walker JL, Gold MA, Smith KM, Zuna RE, Mathews C, et al. Multiple biopsies and detection of cervical cancer precursors at colposcopy. J Clin Oncol 2015;33(1):83–9.
[8] Kitchener HC, Almonte M, Wheeler P, Desai M, Gilham C, Bailey A, et al. HPV testing in routine cervical screening: cross sectional data from the ARTISTIC trial. Br J Cancer 2006;95(1):56–61.
[9] Ronco G, Giorgi-Rossi P, Carozzi F, Confortini M, Dalla Palma P, Del Mistro A, et al. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. Lancet Oncol 2010;11(3):249–57.
[10] Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J, et al. American cancer society, american society for colposcopy and cervical

pathology, and american society for clinical pathology screening guidelines for the prevention and early detection of cervical cancer. Am J Clin Pathol 2012;137:516–42.
[11] Ferris DG, Litaker MS. ALTS Group: prediction of cervical histologic results using an abbreviated Reid Colposcopic Index during ALTS. Am J Obstet Gynecol 2006;194(3):704–10.
[12] Moss S, Gibney A. HPV Primary Screening Pilots: Evaluation report to the National Screening Committee. Available at: legacy.screening.nhs.uk/policy-db_download.php?doc=560 [accessed 18 07.16].
[13] Jeronimo J, Massad S, Schiffman M, et al. Visual appearance of the uterine cervix: correlation with human papillomavirus detection and type. Am J Obstet Gynecol 2007;197:47 e1-47. e8.
[14] van der Marel J, van Baars R, Quint WGV, Berkhof J, del Pino M, Torne A, et al. The impact of human papillomavirus genotype on colposcopic appearance: a cross-sectional analysis. BJOG 2014;121:1117–26.
[15] Pretorius RG, Zhang W-H, Belinson JL, Huang M-N, Wu L-Y, Zhang X, et al. Colposcopically directed biopsy, random cervical biopsy, and endocervical curettage in the diagnosis of cervical intraepithelial neoplasia II or worse. Am J Obstet Gynecol 2004;191(2):430–4.
[16] Sellors J, Qiao Y, Bao Y, Ren S, Lim J, Zhao F, et al. False-negative colposcopy: quantifying the problem. In Book of abstracts of the 22nd International HPV Conference and Clinical Workshop 2005 Apr 30 2005;30.
[17] Balasubramani L, Brown BH, Healey J, Tidy JA. The detection of Cervical Intraepithelial Neoplasia by electrical impedance spectroscopy: the effects of acetic acid and tissue homogeneity. Gynecol Oncol 2009;115:267–71.
[18] Bornstein J, Bentley J, Bösze P, Girardi F, Haefner H, Menton M, et al. 2011 terminology of the international federation for cervical pathology and colposcopy. Obstet Gynecol 2012;120:166–72.
[19] NHS Cervical Screening Programme Colposcopy and Programme Management NHSCSP Publication number 20. Public Health England. Available at: https://www.bsccp.org.uk/assets/file/uploads/resources/NHS_Cervical_Screeing_-Programme._Publication_Number_20_-_Third_Edition.pdf [accessed 20.07.16].
[20] Castle PE, Stoler MH, Wright Jr. TC, Sharma A, Wright TL, Behrens CM. Performance of carcinogenic human papillomavirus (HPV) testing and HPV16 or HPV18 genotyping for cervical cancer screening of women aged 25 years and older: a subanalysis of the ATHENA study. Lancet Oncol 2011;12(9):880–90.
[21] Jeronimo J, Bansil P, Valdez M, Kang L-N, Zhao F-H, Qiao Y-L, et al. The influence of human papillomavirus genotypes on visual screening and diagnosis of cervical precancer and cancer. J Low Genit Tract Dis 2015;19(3):220–3.
[22] Porras C, Wentzensen N, Rodriguez AC, Morales J, Burk RD, Alfaro M, et al. Switch from cytology-based to HPV-based cervical screening: implications for colposcopy. Int J Cancer 2012;130(8):1879–87.
[23] Cantor SB, Cardenas-Turanzas M, Cox DD, Atkinson EN, Nogueras-Gonzalez GM, et al. Accuracy of colposcopy in the diagnostic setting compared with the screening setting. Obstet Gynecol 2008;111(1):7–14.
[24] Zaal A, Louwers J, Berkhof J, Kocken M, ter Harmsel W, Graziosi G, et al. Agreement between colposcopic impression and histological diagnosis among human papillomavirus type 16-positive women: a clinical trial using dynamic spectral imaging colposcopy. BJOG 2012;119:537–44.
[25] Coronado PJ, Fasero M. Colposcopy combined with dynamic spectral imaging: a prospective clinical study. Eur J Obstetr Gynecol Reprod Biol 2016;196:11–6.