

## Clinical application of a new evaluation system in CIN2+ assessment

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### Objectives

To improve the quality of population-based screening in resource limited areas, a feasible strategy would be providing gynecologists with an objective method for colposcopy procedure standardization and results interpretation.

R-way (R: Red; w: white; a: abnormal vascular features; y: yellow) is a standardized colposcopic evaluation system based on standard colposcopy procedure. By analyzing the sequentially appeared features ("R", "w", "a", "y"), a preliminary diagnostic result will be drawn along with a suggestion of biopsy regions, if required. R-way system is built to provide gynecologists with a technical assurance for quick CIN2+ lesions location, hopefully contributing to a decreased incidence and mortality of cervical cancer worldwide.

### Methods

#### Materials

- 752 cases referred to colposcopy were diagnosed by R-way evaluation system and confirmed by histopathology.
- Age range 21-82; M age = 41.22±10.46
- 94 trainees trained by R-way evaluation system

#### Excluded cases

- Cell tissue hyperplastic diseases, including cervical polyp, cervical myoma, cervical condyloma acuminatum and cervical Nessler's cyst.
- Obvious cervical inflammatory bleeding and bleeding caused by endometriosis and cervical treatment.
- Vaginal and vulvar lesions.

#### R-way system

Supplemental instructions and materials were added into conventional colposcopy method:

1. Normal Saline test: Evaluating the "Red" (R) features. If the "red" is obvious, mark the corresponding region in a quadrantal diagram on the computer.

2. Acetic acid test: use 5% acetic acid to stain the surface of cervix for 50 seconds, recognize and mark the area appearing acetowhite epithelium at position with epithelium hyperplasia/variation on superficial cervix; the acetowhite epithelium is classified as thick acetowhite epithelium and thin acetowhite epithelium, observe the images of acetowhite epithelium for 1 min and 2 min and compare them, if the thickness of acetowhite epithelium is increased or is being increased, and the acetowhite epithelium is characterized as upheaval, boundary and non-transparence, it is thick acetowhite epithelium; if the acetowhite epithelium doesn't agree with the characteristics of thick acetowhite epithelium, observe and compare the acetowhite epithelium with the image of it in normal saline for 2 min, there still exists thin acetowhite epithelium, and mark the corresponding region in a quadrantal diagram on the computer.
3. Lugol's iodine test: perform Lugol's iodine test to stain the acetowhite epithelium, when the acetowhite epithelium (including thick acetowhite epithelium and thin acetowhite epithelium) appears yellow or mustard yellow, light brown or dark brown, recognize and mark the yellow or mustard yellow area in a quadrantal diagram on the computer
4. If mustard yellow doesn't appear, check the abnormal vessels and recognize and mark the area of abnormal vessels. Observe the staining result of Lugol's iodine test and the abnormal vessels on the acetowhite epithelium.
5. Preliminary diagnostic results: Given by software based on R-way specialized database. Biopsy regions is suggested for positive cases.

#### R-way system training method:

1. Preliminary diagnostic examination of colposcope image was performed before and after three weeks of training using R-way colposcope software.
2. 50 cases in colposcope database was extracted to combine the examination paper according to the histopathological result on cervical cancer, high grade lesion, low grade lesion and chronic cervicitis were in portion of 5:30:10:5

- 3. Make preliminary diagnosis based on colposcope screening images before and after training by R-way software.
- 4. To analysis coincidence rates of R-way diagnosed HSIL and biopsy tissue pathological diagnosis CIN2+ (coincidence rate = correct cases/50)

**Statistic analysis method:**

- SAS9.4 software
- Sensitivity, specificity, PPV, NPV, estimated value of coincidence rate and confidence interval for high grade lesion.
- ROC curve
- Pairing t-test before and after training
- P < 0.05

**Results**

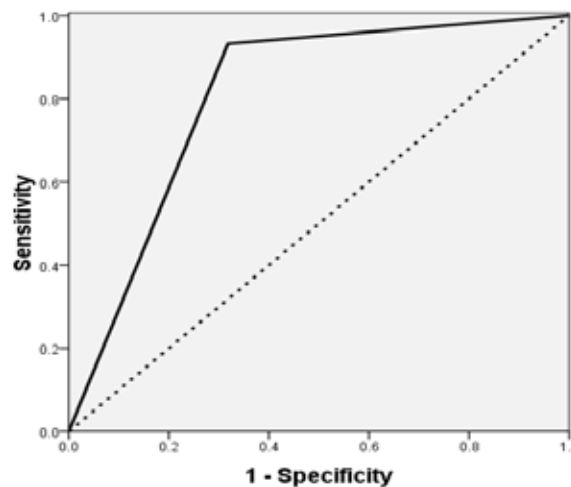
**Evaluating Indicators**

- 752 cases diagnosed with R-way evaluation system
- 50 cases (6.65%) were diagnosed as suspicious for cervical cancer by visual examination
- 252 cases (33.51%) were diagnosed as HSIL
- 288 cases (38.2%) were diagnosed as LSIL
- 162 cases (21.54%) were diagnosed as normal colposcopy findings
- Histopathological results of 752 cases

**The clinical value of R-way to diagnosis high grade lesion:**

- Sensitivity 68.17% (95%CI: 62.98, 72.94)
- Specificity 93.22% (95%CI: 90.19, 95.37)
- Positive predictive value 90.08% (95%CI: 85.77, 93.19)
- Negative predictive value 76.44% (95%CI: 72.31, 80.13)
- Coincidence rate 81.34% (95%CI: 78.29, 84.05)

- Lower area of ROC curve 0.807 (95%CI: 0.773, 0.841)
- Diagnostic significance of cervical cancer (P<0.0001)



AUC of ROC assessed by R-way System for CIN2+

**R-way training outcome:**

- The average coincidence rate (78.28±7.37%) of trainees after training was increased by 14.98% compared with the average coincidence rate (63.30±13.07%) before training, and the difference was of statistical significance through pair t-test (t=9.59, P <0.001).

**Discussions**

- Lack of unified quantitative evaluation standard in the process of conventional colposcopy method, thus subjective factors may influence the evaluation result.

Screening result	Histopathological result										
	Total		Chronic cervicitis		LSIL		HSIL		cervical cancer		
	n	%	n	%	n	%	n	%	n	%	
SCC	50	100	1	2	0	0	11	22	38	76	
R-way	HISL	252	100	18	7.14	7	2.78	224	88.89	3	1.19
	LSIL	288	100	127	44.1	117	40.63	44	15.28	0	0
	NCF	162	100	68	41.98	32	19.75	61	37.65	1	0.62
Total	752	100	214	28.46	156	20.74	340	45.21	42	5.59	

Comparison of Coincidence Rates Before and After Training of Different Groups of Trainees									
Groups	Number of cases	Coincidence rate before training (%)				Coincidence rate after training (%)			
		Average value	Standard deviation	F value	P value	Average value	Standard deviation	F value	P value
>=75%	22	80.09	5.18	213.82	<0.0001	77	5.85	1.86	0.1416
65-75 %	21	69.71	2.78			77.05	6.83		
55-64%	25	59.6	2.89			81.2	8.39		
55%	26	47.46	6.44			77.54	7.53		

- Through time control, the R-way evaluation system recognizes each images captured color and marks the focus of infections strictly follows colposcopy screening procedure standards
- During colposcopy, by applying 5% dilute acetic acid solution and Lugol's solution , images were captured by colposcope for further analysis. Those images were formed by the light which reflected from the stroma underlying the epithelial cells. By observation and analysis of image features such as the color, shape, border and vessels, HSIL could be detected.
- The R-way system can decrease the effect of personnel factors on preliminary diagnosis by colposcope and accurate the focus of biopsy location so as to avoid unnecessary false positive or false negative result. To provide better consistency of clinical results done by different education level doctors
- In low resource countries, it is difficult to locate the CIN2+ in a short period. Meanwhile, for most colposcopists, especially primary colposcopist in rural areas, the accuracy and consistency of preliminary results greatly varied from case to case. With the R-way system, standardized colposcopic examination procedure could help the gynecologists to quick grasp of colposcopy technology and to detect CIN2+.
- The coincidence rate of trainees for cervical lesions diagnosis was improved obviously through training with R-way system and trainees skill after training were identical, which indicates R-way is a feasible education program for clinical users.

### Conclusions

- Through time control of colposcopy procedure, the R-way system standardizes the time point of each images captured, identifies the color changes (red, white and yellow) in each step and evaluates the presence of transformation zone.
- For its ease of use and standardized management of colposcopy procedure, R-way system is highly recommended for cervical cancer screening.
- The R-way system provide a standardized evaluation procedure that to consistence the preliminary diagnostic results issued by different level educated clinical users, meanwhile

### References

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2. Dong ZW, Qiao YL, Kong LZ, et al. The Strategy and Implementation for Early Detection of Cancer in China .China Cancer (2008), 17(4):263-5.