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# Evaluation of a real-time optoelectronic method for the detection of cervical intraepithelial neoplasia and cervical cancer in patients with different transformation zone types

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**We aimed to evaluate the diagnostic value of TruScreen, a real-time diagnostic technology, for cervical lesions in patients with different transformation zone (TZ) types. A total of 1908 women aged 34.0 ± 7.3 years who have received cytology, human papillomavirus (HPV) testing, TruScreen, and colposcopy were recruited. The clinical performances of these tests were evaluated for their detection of high-grade squamous intraepithelial lesion (HSIL), adenocarcinoma in situ (AIS), or more severe lesions in patients with different TZ types. For the detection of HSIL, AIS, or more severe lesions, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of TruScreen were 65.08%, 64.76%,11.55%, and 96.33%, respectively, which were similar to cytology (all *P* values > 0.05). For the detection of HSIL + in patients with type 3 TZ, the sensitivity, specificity, PPV, and NPV of TruScreen were 72.29%, 67.59%, 13.86%, and 97.13%, respectively, which were significantly higher than the sensitivity (51.16%, *P* = 0.029), specificity (59.59%, *P* = 0.001), PPV (7.94%, *P* = 0.016), and NPV (94.71%, *P* = 0.049) in type 1 and type 2 TZs. TruScreen has detection accuracy comparable to cytology and performs even better in patients with type 3 TZ.**

**Keywords** TruScreen, Optoelectronic device, Transformation Zone, Human papillomavirus (HPV), High-grade squamous intraepithelial lesion (HSIL), Colposcopy

Cervical cancer, mainly caused by high-risk (HR) human papillomavirus (HPV) infection, is one of the most common malignant tumors in women and is the fourth leading cause of cancer-related death in women worldwide[1]. In 2020, there were more than 600,000 new cases of cervical cancer, of which about 342,000 died of this cancer worldwide[1]. The World Health Organization (WHO) 90-70-90 targets (90% of fully vaccinated girls by the age of 15 years, 70% of females undergoing cervical cancer screening by high-performance test at 35 and 45 years of age, and treatment for 90% of women identified with cervical disease) are aimed to prevent more than 62 million cervical cancer-related deaths by the year 2120[2]. Currently, the commonly used screening methods for cervical cancer include HPV and cytological testing[3].

A field that is dynamically entering the prevention and diagnosis of cervical lesions is biophysics and molecular biology. The electrical impedance spectroscopy (EIS) of the University of Sheffield assesses impedance, which consists of the capacitance and electrical resistance of the cervical epithelium. It offers prognostic information on the risk of high-grade squamous intraepithelial lesion (HSIL) + developing over three years following EIS measurements[4]. Shukla et al. reported a portable device that works on extracting intrinsic fluorescence from tissue samples using the measured polarized fluorescence and elastic scattering spectra on a smartphone camera[5].

A real-time optoelectronic (TruScreen) method has been introduced in the screening and diagnosis of cervical lesions for a few years in China and many other countries[6–10]. This innovative approach analyzes the cervical mucosa by measuring the response to a light beam and electric potential, which includes reflected, scattered light, and electrical impulses. The method is automated to minimize human error and is based on comparing

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patient data with a standard derived from a diverse control group of 3,000 women. The optoelectronic method examines direct reflection, backscatter, and charge dissipation. These provide information about the cervical surface's topography and the properties of the epithelial layers. The method also evaluates the electrical properties of tissues, including the cytoplasm's complex electrolyte nature, the cell membrane's capacitive behavior, and the semiconductor function of other cellular elements. The electrical impedance, or the combined resistance and phase shift of the current, varies between normal and pathologically changed tissues. The optoelectronic equipment measures the returning light and electrical response, and analyzes cervical tissues with a built-in algorithm[11–14]. The test results are categorized as "normal" or "abnormal". TruScreen is designed to be used by an operator without high levels of technical skill or training[14]. The advantages of this technology were its immediate and objective results[7]. Although TruScreen has been used clinically for many years, the existing literature mainly focused on its role as a screening method, with varying sensitivity and specificity[7,8,14–16]. None, to the best of our knowledge, have some data on the effectiveness of TruScreen for detecting HSIL, adenocarcinoma in situ (AIS), and more severe lesions with different transformation zone (TZ) types.

Our study aimed to evaluate the clinical value of TruScreen in the diagnosis of HSIL + cervical lesions by comparing the diagnostic performances of TruScreen, liquid-based cytology, HPV testing, and colposcopic impression for the detection of cervical HSIL or more severe cases, and in particular, the detection ability of these methods in patients with different TZ types.

## Methods

The study was conducted on 1908 women aged 18–60 (34.0 ± 7.3) years consecutively referred to colposcopy by abnormal liquid-based cytology results with or without persistent HR-HPV infection. Exclusion criteria included a cervical procedure such as a biopsy, laser cauterization, photodynamic treatment, or conization within the previous three months, prior history of pelvic radiation therapy or chemotherapy, history of hysterectomy or trachelectomy, current menstrual period during the examination period, gestation or < 42 days postpartum, inability to cooperate with the examination for any reason. The liquid-based cytology and HPV testing were performed at least 1 week earlier. The patients underwent a cervical examination with a TruScreen real-time optoelectronic scanner, and following that, a colposcopy was performed. Only those with colposcopy-directed punch biopsy results were included in this study.

### TruScreen testing

The Second generation of TruScreen (Polartechnics, Sydney, Australia) is a real-time device that uses electrical and optical signals to classify cervical tissue using an expert system approach. The distal tip of the handpiece is covered with a 5-mm diameter single-use sensor (SUS) element designed to protect against cross-infection. The SUS is a pen-like wand covered by a disposable sensor that gently touches multiple spots on the cervix. The sensor contains a precision lens and electrodes that interface with the cervix, sending and picking up low-level electrical and optical signals from the cervical tissue. These signals are then analyzed by an integrated AI-enabled algorithm, providing objective results immediately. The device uses a combination of biosensors, including directly reflected light, backscattered light, and electrical decay curves. The operator used the handpiece to target at least 15 sites of the cervical surface. During the examination, the "stop/go" lights on the handpiece tell the operator to move the probe tip to a tissue spot, stop for the measurement to be performed, and then proceed to the next spot. This sequence is repeated until the ectocervix and the portion of the lower endocervix exposed by the vaginal speculum have been covered[10]. The results were obtained in real-time and defined as: (1) Normal (no abnormal cervical cells were found) or (2) Abnormal (abnormal cells were found in the cervix). This test causes no trauma or pain to the patient and lasts only about 2–3 min.

## Liquid-based cytology

Cervical samples were subjected to liquid-based cytology in the pathology laboratory. Two pathologists reviewed the results before reporting them. The results were analyzed using the third edition of the Bethesda system[17] and graded as negative intraepithelial lesion or malignancy (NILM), atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), HSIL, atypical squamous cells-cannot exclude HSIL (ASC-H), atypical glandular cells (AGC), or LSIL cannot exclude HSIL (LSIL-H).

## HPV testing

The liquid samples collected by the clinicians were tested with the Cobas HPV assay (Roche Diagnostics; Indianapolis, IN, USA)[18] or HPV genotyping utilizing the BioPerfectus Multiplex Real-Time PCR assay (BioPerfectus Technology Co, Taizhou, China), detecting 21 HPV genotypes, including 18 high risk and possibly high-risk HPV genotypes (HPV 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82) and 3 low-risk HPV genotypes (HPV 6, 11, and 81)[19].

## Colposcopy and cervical biopsy

The cervix was consecutively examined using 3% acetic acid and 5% Lugol's solution and observed with a magnification microscope. The 2011 International Federation for Cervical Pathology and Colposcopy (IFCPC) classification[20] was adopted for our colposcopy reports. Colposcopy-directed biopsy was performed when lesions were detected by colposcopy, the TZ was type 3 (endocervical curettage), or when there were other clinical indications for biopsy. Generally, 1–4 biopsies were taken for each patient according to the colposcopic impression. Among our 1908 cases, 144 (7.55%) took one biopsy, 979 (51.15%) took two biopsies, 490 (25.68%) took three biopsies, and 295 (15.46%) took four biopsies. Two senior attending pathologists reviewed the pathological sections before being reported. The pathology reports were based on Lower Anogenital Squamous

Terminology (LAST)/World Health Organization (WHO) recommendations, and for reporting histologic HSIL, the pathologists included cervical intraepithelial neoplasia (CIN) 2 or CIN3 qualifiers, for example, HSIL (CIN2) and HSIL (CIN3)[21,22]. The histopathological results were accepted as a gold standard.

## Combined screening method

All the patients recruited had both liquid-based cytology and HPV tests before colposcopy. The indication of colposcopy referral was considered the positive criterion for combined screening methods, following the 2012 American Society for Colposcopy and Cervical Pathology (ASCCP) consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors[23]. When HPV genotyping combined with cytology was performed, the criteria for referral to colposcopy were HPV16/18-positive, persistent other HR-HPV positive for over 1 year with cytology NILM, HR-HPV-positive with cytology ASC-US or more severe.

## Statistical analysis

The SPSS software (IBM Corp. Released 2015. Version 23.0. Armonk, NY, USA) was used to process data. Each screening method's sensitivity, specificity, PPV, and NPV were calculated using pathologically confirmed cervical HSIL as the gold standard. Exact Fisher's $X^2$ test was used to compare differences between groups. $P < 0.05$ was recognized as statistically significant.

# Results

## General characteristics

There were 1908 subjects included in the study, with an average age of $34.0 \pm 7.3$ years. The liquid-based cytology results distribution were: 1203 cases with normal results, 384 cases of ASC-US, 277 patients of LSIL, 41 cases of HSIL/ ASC-H, 2 cases of AGC, and 1 case of LSIL-H. HR-HPV infection was detected in 1727 cases. Pathological results showed that there were 126 (6.60%) CIN 2 + cases, including 115 (6.03%) CIN2 and CIN3 cases, 5 (0.26%) AIS cases, and 5 (0.26%) cervical cancer cases. There were 499 (26.15%) HPV 16/18 positive, 705 (36.95%) liquid-based cytology tests with ASC-US or worse, 626 HR-HPV positive and cytology ASC-US or worse, 805 persistence other HR-HPV positive for over 1 year, 307 (16.09%) colposcopic impression of HSIL or worse, and 710 (37.21%) TruScreen tests abnormal cases among the 1908 subjects (Table 1).

## TruScreen testing results

The positive rate of TruScreen markedly increased with increasing severity of liquid-based cytology results, from 30.92% (372/1203) in women with NILM to 100% (25/25) in women with HSIL. Similarly, this rate increased from 28.69% (338/1178) in women with normal histology results, 48.01% (290/604) LSIL, 63.79% (74/116) HSIL, 60% (3/5) AIS, and 100% (4/4) cervical cancer, respectively.

## Diagnostic performance of TruScreen in the detection of cervical HSIL, AIS, or more severe lesions

For the detection of HSIL, AIS, or more severe lesions, the specificity of TruScreen (64.76%) was significantly higher than that of HPV testing (10.10%, $P = 0.000$), but similar to liquid-based cytology (64.47%, $P = 0.889$), and

| | Total (%) | Normal (%) | LSIL (%) | HSIL (%) | AIS (%) | Cancer (%) |
|---|---|---|---|---|---|---|
| HR-HPV | | | | | | |
| Negative | 181 (9.49) | 135 (11.46) | 45 (7.45) | 1 (0.86) | 0 | 0 |
| HPV16/18+ | 499 (26.15) | 275 (23.34) | 149 (24.67) | 65 (56.03) | 5 (100) | 5 (100) |
| Non-HPV 16/18+ | 1228 (64.36) | 768 (65.20) | 410 (67.88) | 50 (43.10) | 0 | 0 |
| Cytology | | | | | | |
| NILM | 1203 (63.05) | 866 (73.51) | 283 (46.85) | 51 (42.71) | 2 (40) | 1(20) |
| ASC-US | 384 (20.13) | 217 (18.42) | 147 (24.34) | 18 (15.63) | 2 (40) | 0 |
| LSIL or worse | 321 (16.82) | 95 (8.06) | 174 (28.81) | 47 (41.67) | 1 (20) | 4 (80) |
| Colposcopic impression | | | | | | |
| Normal | 597 (31.29) | 489 (41.51) | 98 (16.63) | 8 (6.90) | 2 (40) | 0 |
| LSIL | 1005 (52.67) | 576 (48.90) | 397 (65.73) | 31 (26.72) | 1 (20) | 0 |
| HSIL or worse | 306 (16.04) | 113 (9.62) | 109 (18.05) | 77 (66.38) | 2 (40) | 5 (100) |
| TruScreen | | | | | | |
| Normal | 1198 (62.79) | 840 (71.31) | 314 (51.99) | 42 (36.21) | 2 (40) | 0 |
| Abnormal | 710 (37.21) | 338 (28.69) | 290 (48.01) | 74 (63.79) | 3 (60) | 5 (100) |
| Total | 1908 | 1178 (61.74) | 604 (31.66) | 116 (6.08) | 5 (0.26) | 5 (0.26) |

**Table 1**. Distribution of HR-HPV, liquid-based cytology, colposcopic impression, and TruScreen by histological results among 1908 women. HR-HPV: high-risk human papillomavirus; NILM: negative intraepithelial lesion or malignancy; ASC-US: atypical squamous cells of undetermined significance; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; AIS: adenocarcinoma in situ.

| | HPV testing | | Liquid-based cytology | | Colposcopic impression | | TruScreen | |
|---|---|---|---|---|---|---|---|---|
| | No. of Positive/N | Estimate% | No. of Positive/N | Estimate% | No. of Positive/N | Estimate% | No. of Positive/N | Estimate% |
| Threshold | HR-HPV positive | | ASC-US+ | | HSIL | | Abnormal | |
| Detection of HSIL, **AIS**, or more severe lesions ($n=126$) | | | | | | | | |
| Sensitivity | 125/126 | 99.21 | 72/126 | 57.14 | 84/126 | 66.67 | 82/126 | 65.08 |
| Specificity | 180/1782 | 10.10 | 1149/1782 | 64.47 | 1559/1782 | 87.49 | 1154/1782 | 64.76 |
| PPV | 125/1727 | 7.24 | 72/705 | 10.21 | 84/307 | 27.36 | 82/710 | 11.55 |
| NPV | 180/181 | 99.45 | 1149/1203 | 95.51 | 1559/1601 | 97.38 | 1154/1198 | 96.33 |

**Table 2**. Clinical performance of HPV testing, liquid-based cytology, colposcopic impression, and TruScreen for the detection of HSIL, AIS, or more severe lesions. PPV: positive predictive value; NPV: negative predictive value; HR-HPV: high-risk human papillomavirus; ASC-US: atypical squamous cells of undetermined significance; HSIL: high-grade squamous intraepithelial lesion; AIS: adenocarcinoma in situ.

| | HR-HPV(+) with TruScreen | | HR-HPV(+) with cytology | | *P* value |
|---|---|---|---|---|---|
| | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% | |
| Threshold | Normal TS with HPV16/18 positive, or abnormal TS with HR-HPV-positive | | NILM of cytology with HPV16/18 positive, or ASCUS + of cytology with HR-HPV-positive | | |
| Positive | 656/1727 | 37.98 | 612/1727 | 35.44 | |
| Detection of HSIL, AIS, or more severe lesions ($N=125$ ) | | | | | |
| Sensitivity | 81/125 | 64.80 | 72/125 | 57.60 | 0.243 |
| Specificity | 1027/1602 | 64.11 | 1062/1602 | 66.29 | 0.194 |
| PPV | 81/656 | 12.35 | 72/612 | 11.76 | 0.750 |
| NPV | 1027/1071 | 95.89 | 1062/1115 | 95.25 | 0.464 |

**Table 3**. Clinical performance of HPV genotyping combined with TruScreen or cytology in HR-HPV-positive women for detection of HSIL, AIS, or more severe lesions. TS: TruScreen; PPV: positive predictive value; NPV: negative predictive value; HR-HPV: high-risk human papillomavirus; NILM: negative intraepithelial lesion or malignancy; ASC-US: atypical squamous cells of undetermined significance; HSIL: high-grade squamous intraepithelial lesion; AIS: adenocarcinoma in situ.

significantly lower than colposcopic impression (87.49%, $P=0.000$). Additionally, the sensitivity of TruScreen was 65.08%, which was similar to the colposcopic impression (66.67%, $P=0.894$) and liquid-based cytology (57.14%, $P=0.245$), but significantly lower than HPV testing (99.21%, $P=0.000$). The positive predictive value (PPV) of TruScreen (11.55%) was significantly higher than that of HPV testing (7.24%, $P=0.001$), similar to liquid-based cytology (10.21%, $P=0.443$), and significantly lower than colposcopic impression (27.36%, $P=0.000$). The negative predictive value (NPV) of TruScreen (96.33%) was significantly lower than HPV testing (99.45%, $P=0.023$), but similar to liquid-based cytology (95.51%, $P=0.353$), and colposcopic impression (97.38%, $P=0.122$) (Table 2). Truscreen showed higher specificity and PPV when compared with HPV testing, but lower specificity and PPV than colposcopic impression, and lower NPV than HPV testing.

## Diagnostic performance of a combination of HR-HPV testing and TruScreen to detect cervical HSIL, AIS, or more severe lesions

Women with HR-HPV-positive results were further triaged by TruScreen or cytology. HR-HPV-positive women further triaged with TruScreen had a similar positive rate as with the current cervical cancer screening strategy based on cytology triage for HR-HPV primary screening (Table 3). For detection of cervical HSIL, AIS, or more severe lesions in HR-HPV-positive women, the sensitivity, specificity, PPV, and NPV of women triaged with TruScreen (64.8%, 64.11%, 12.35%, and 95.89% respectively) was similar with HR-HPV-positive women triaged with TCT (57.6%, 66.29%, 11.76%, 95.25%, respectively, all $P$ values > 0.05, Table 3).

## Diagnostic performance of TruScreen in the detection of cervical HSIL, AIS, or more severe lesions in patients with type 3 TZ

Among the 1908 subjects, 1234 had a type 3 TZ. For the detection of HSIL, AIS, or more severe cervical lesions in these patients, the specificity of TruScreen (67.59%) was significantly higher than that of HPV testing (11.03%, $P=0.000$), but similar to liquid-based cytology (64.29%, $P=0.104$), and significantly lower than colposcopic impression (90.00%, $P=0.000$). Additionally, the sensitivity of TruScreen was 72.29%, which was similar to the colposcopic impression (68.67%, $P=0.734$) and liquid-based cytology (65.06%, $P=0.403$), but significantly lower than HPV testing (98.80%, $P=0.000$). The PPV of TruScreen (13.86%) was significantly higher than that of HPV testing (7.41%, $P=0.000$), but similar to liquid-based cytology (11.61%, $P=0.318$), and significantly lower than colposcopic impression (33.14%, $P=0.000$). The NPV of TruScreen (97.13%) was similar to that of HPV

| | HPV testing | | Liquid-based cytology | | Colposcopic impression | | TruScreen | |
|---|---|---|---|---|---|---|---|---|
| | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% |
| Threshold | HR-HPV positive | | ASC-US+ | | HSIL | | Abnormal | |
| Detection of HSIL, AIS, or more severe lesions ($n=83$) | | | | | | | | |
| Sensitivity | 82/83 | 98.80 | 54/83 | 65.06 | 57/83 | 68.67 | 60/83 | 72.29 |
| Specificity | 127/1151 | 11.03 | 740/1151 | 64.29 | 1036/1151 | 90.00 | 778/1151 | 67.59 |
| PPV | 82/1106 | 7.41 | 54/465 | 11.61 | 57/172 | 33.14 | 60/433 | 13.86 |
| NPV | 127/128 | 99.22 | 740/769 | 96.23 | 1036/1062 | 97.55 | 778/801 | 97.13 |

**Table 4**. Clinical performance of HPV testing, liquid-based cytology, colposcopic impression, and TruScreen for the detection of HSIL, AIS, or more severe lesions in patients with type 3 transformation zone. PPV: positive predictive value; NPV: negative predictive value; HR-HPV: high-risk human papillomavirus; ASC-US: atypical squamous cells of undetermined significance; HSIL: high-grade squamous intraepithelial lesion; AIS: adenocarcinoma in situ.

| | HPV testing | | Liquid-based cytology | | Colposcopic impression | | TruScreen | |
|---|---|---|---|---|---|---|---|---|
| | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% | No. of Positive/*N* | Estimate% |
| Threshold | HR-HPV positive | | ASC-US+ | | HSIL | | Abnormal | |
| Detection of HSIL, AIS, or more severe lesions ($n=43$) | | | | | | | | |
| Sensitivity | 43/43 | 100 | 18/43 | 41.86 | 27/43 | 62.79 | 22/43 | 51.16 |
| Specificity | 54/631 | 8.56 | 409/631 | 64.82 | 522/631 | 82.73 | 376/631 | 59.59 |
| PPV | 43/620 | 6.94 | 18/240 | 7.50 | 27/136 | 19.85 | 22/277 | 7.94 |
| NPV | 54/54 | 100 | 409/434 | 94.24 | 522/538 | 97.03 | 376/397 | 94.71 |

**Table 5**. Clinical performance of HPV testing, liquid-based cytology, colposcopic impression, and TruScreen for the detection of HSIL, AIS, or more severe lesions in patients with type 1 and type 2 transformation zones. PPV: positive predictive value; NPV: negative predictive value; HR-HPV: high-risk human papillomavirus; ASC-US: atypical squamous cells of undetermined significance; HSIL: high-grade squamous intraepithelial lesion; AIS: adenocarcinoma in situ.

testing (99.22%, $P=0.234$), liquid-based cytology (96.23%, $P=0.328$), and colposcopic impression (97.55%, $P=0.661$) (Table 4). In patients with type 3 TZ, TruScreen showed higher specificity and PPV compared with HPV testing, but lower specificity and PPV than colposcopic impression.

### Diagnostic performance of TruScreen in the detection of cervical HSIL, AIS, or more severe lesions in patients with type 1 and type 2 TZs

Among the 1908 subjects, 416 were with type 1 TZ, and 258 were with type 2 TZ. For the detection of HSIL, AIS, or more severe lesions with type 1 and type 2 TZs, the specificity of TruScreen (59.59%) was significantly higher than that of HPV testing (8.56%, $P=0.000$), but similar to liquid-based cytology (64.82%, $P=0.063$), and significantly lower than colposcopic impression (82.73%, $P=0.000$). Additionally, the sensitivity of TruScreen was 51.16%, which was significantly lower than HPV testing (100%, $P=0.000$), but similar to liquid-based cytology (41.86%, $P=0.517$) and colposcopy impression (62.79%, $P=0.384$). The PPV of TruScreen (7.94%) was similar to HPV testing (6.94%, $P=0.580$) and liquid-based cytology (7.50%, $P=0.871$), but significantly lower than colposcopic impression (19.85%, $P=0.001$). The NPV (94.71%) of TruScreen was similar to that of HPV testing (100%, $P=0.157$), liquid-based cytology (94.24%, $P=0.880$), and colposcopic impression (97.03%, $P=0.089$) (Table 5).

In patients with type 1 and type 2 TZs, TruScreen showed higher specificity than HPV testing, lower specificity, and PPV than colposcopic impression, and lower sensitivity than HPV testing. Interestingly, we also found that TruScreen showed some strength in the detection of HSIL, AIS or more severe lesions for patients with type 3 TZ, even higher than its performance in type 1 and type 2 TZs, with significantly higher sensitivity ($P=0.029$), specificity ($P=0.001$), PPV ($P=0.016$), and NPV ($P=0.049$).

## Discussion

More than 85% of cervical cancers are detected in low-income and middle-income countries[24], which resulted from the comparatively low coverage of the HPV vaccine and cervical cancer screening[25]. Liquid-based cytology and HPV DNA or mRNA testing are the 2 main screening methods. However, they both take some time to get the results, which vary from several days to several weeks, by different centers. A comparatively new screening method, TruScreen, with its advantage of instant results, has come to the attention of many clinicians. In this study, with data analysis from our center, we found that TruScreen has a screening accuracy generally comparable to liquid-based cytology, and its strength is even more apparent in patients with type 3 TZ.

TruScreen is a real-time optoelectronic intelligent technology for the screening of cervical cancer[26]. It is an objective, self-checking digital system that can be used by medical staff with minimal training. Unlike liquid-based cytology or HPV testing, this technology requires little infrastructure and resources, and no cytologist[27]. The role of TruScreen in cervical cancer screening has been reported in many clinical studies, with a sensitivity varying from 43 to 76% and specificity varying from 53 to 92% for detecting HSIL+ cervical lesions[9,14,28–30]. In our study, the performance of TruScreen for screening and triage of HR-HPV-positive women was comparable to liquid-based cytology, consistent with previous reports[31]. Currently, there are 3 available cervical cancer screening strategies: primary HPV screening, co-testing with HPV testing and cervical cytology, and cervical cytology alone[22]. The excellent performance of TruScreen gives us an option of replacing liquid-based cytology screening with TruScreen in areas with limited resources[7]. However, in centers with qualified cytologists, the liquid-based cytology could provide us with more valuable information than TruScreen, since the results we get from TruScreen are with two tiers and are only classified as "normal" or "abnormal". In contrast, the cytology results have multiple tiers, providing more information to estimate the risk of HSIL, AIS or more severe lesions. Therefore, cytology still serves an irreplaceable role in cervical cancer screening, while TruScreen provides an option in low resource areas.

We also evaluated the performance of colposcopic impressions. Published data consistently reported a large variability in sensitivity and specificity, with values ranging from 30 to 90% and 40-95%, respectively[32]. Our center has highly trained colposcopists, each performing more than 1000 colposcopies yearly, and their performances are appraised monthly. Therefore, the sensitivity and specificity of our colposcopic impression are comparatively high, 66.67% and 87.49%, respectively. Colposcopy is an essential diagnostic tool for cervical intraepithelial neoplasia and cervical cancer, but is not generally used as a screening tool. What surprised us was that the sensitivity for HSIL, AIS, or more severe lesions of TruScreen in patients with type 3 TZ was even higher than the colposcopic impression, although the difference was insignificant.

Our study further evaluated the clinical performance of TruScreen for detecting HSIL, AIS, or more severe lesions in patients with different TZ types. Interestingly, TruScreen performed better in patients with type 3 TZ than those with type 1 and type 2 TZs. The reason for this phenomenon may be attributed to the fact that the TruScreen sensor could be pointed into the external cervical os and get more information from the cervical canal, which consequently improves the detection accuracy. During TruScreen examination, tissue is illuminated at four discrete wavelengths in the visible and infrared regions of the spectrum. Furthermore, TruScreen incorporates electrical measurements of decay curves where the rate of electrical decay is inversely proportional to the degree of abnormality on the cervix[10]. However, for liquid-based cytology, if the external cervical os were too small or even closed, it is challenging to acquire cell samples from the cervical canal. Also, during colposcopic examination, we cannot perceive the cervical canal and may only appraise its condition by endocervical curettage.

This study also had a few limitations. First, TruScreen was not performed simultaneously with liquid-based cytology or HPV testing, which may have resulted in a biased observation. Second, the sensitivity of liquid-based cytology for patients with type 1 and type 2 TZs was only 41.86%. Since our center is one of the best centers in China, and we have many referrals from primary medical institutions that don't have enough well-qualified cytologists, the accuracy of their liquid-based cytology results might be compromised.

In conclusion, TruScreen, as a real-time technology, has detection accuracy comparable to liquid-based cytology and performs even better in patients with type 3 TZ.

## Data availability

The datasets generated for this study are available upon written request to the corresponding author.

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## Author contributions

Conceptualization, L.S. and F.X.; methodology, L.S. and F.X.; writing-original draft preparation, F.X.; writing-review and editing, L.S. Both authors have read and agreed to the published version of the manuscript.

## Declarations

## Competing interests

The authors declare no competing interests.

## Ethical considerations

This study was carried out according to the principles in the Declaration of Helsinki 1964 and all subsequent revisions. It was approved by the institutional ethics review board of the Obstetrics and Gynecology Hospital of Fudan University. Informed consent was obtained from all individual participants included in the study.

## Additional information

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