Original Article

Implementation of the Thinprep Imaging System in a Tertiary Military Medical Center

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BACKGROUND: The ThinPrep Imaging System (TIS) was implemented at Brooke Army Medical Center (BAMC) in February 2006 and has been a crucial part of the ability of the Department of Pathology and Laboratory Services ability to improve efficiency and turnaround times for Papanicolaou (Pap) test reporting. The increased detection rate of squamous abnormalities, specifically high-grade squamous intraepithelial lesions (HSIL), has been well documented by many studies. In addition, the TIS has increased productivity for many laboratories. The objective of this study was to evaluate the effects of implementing the TIS at BAMC, a tertiary military medical center. Specifically, the following were assessed: 1) whether the detection of squamous abnormalities was increased with the TIS, 2) how the rate of high-risk human papillomavirus (HR-HPV) detection in atypical squamous cells (ASC) of undetermined significance (ASC-US) cases changed (or did not change) before and after implementation of the TIS, and 3) how the TIS influenced productivity. **METHODS:** All gynecologic cytology at BAMC has been collected and processed using the ThinPrep system since 2002. Before February 2006 and before implementation of the TIS, Pap tests were screened manually by the cytotechnologists. Detection rates of squamous abnormalities were compared between the period from February 2005 to December 2005 (manual screening) and the period from February 2006 to December 2006 (image-assisted screening). Squamous abnormalities included ASC-US; ASC, cannot rule out HSIL (ASC-H); low-grade squamous intraepithelial lesion (LSIL); HSIL; glandular abnormalities; and malignancies (squamous or glandular). In addition, the rates of HR-HPV-positive, HR-HPV-negative, and HR-HPV-quantity not sufficient were compared for the same periods. During both periods, testing for HR-HPV was performed only on ASC-US Pap tests. HR-HPV was tested with Digene Hybrid Capture 2 methodology. Productivity was calculated as the change in average slides screened per hour before and after imager implementation. **RESULTS:** In total, 107,647 Pap tests were analyzed in the 2005 (54,438 Pap tests) and 2006 (53,209 Pap tests) timeframes. Increases in the detection of ASC-H, atypical glandular cells (AGC), LSIL, and HSIL were statistically significant. The proportion of negative for intraepithelial lesion or malignancy (NILM) and unsatisfactory cases decreased significantly with implementation of the TIS. The ASC to squamous intraepithelial lesion (ASC:SIL) ratio decreased from 1.5 to 1.0 after TIS implementation. Decreases in the ASC-US HR-HPV-positive proportion and increases in the ASC-US HR-HPV-negative proportion after implementation of the TIS were statistically significant. In our laboratory, a 60% increase in productivity was noted with use of the TIS. **CONCLUSIONS:** Implementation of the TIS at

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BAMC significantly increased the detection of ASC-H, AGC, LSIL, and HSIL but had no significant impact on the ASC-US detection rate. Although the ASC-US rate did not change, both the HR-HPV-positive rate and the ASC:SIL ratio decreased. The data from the current study suggested that, at least initially, the use of imager-directed screening may increase the number of clinically insignificant ASC-US Pap tests. **Cancer (Cancer Cytopathol) 2009;117:264–70. Published 2009 by the American Cancer Society.***

KEY WORDS: atypical squamous cells of undetermined significance, liquid-based Papanicolaou test, high-risk human papillomavirus, ThinPrep Imaging System, cervical screening.

Cervical cancer screening (the Papanicolaou [Pap] test) has been 1 of the most successful cancer prevention programs ever developed. Despite this success, the cytology community continually has sought to improve it as new technologies have become available. With the introduction of liquid-based processing, the addition of computer-assisted screening into routine practice became possible.[1] Unlike some prior systems in which the goal was full automation, the ThinPrep Imaging System (TIS) (Hologic Corporation [previously Cytyc Corporation], Marlborough, Mass) was designed to assist, not replace, the cytotechnologist.[2] The TIS combines imaging technology with human interpretation to aid in Pap test evaluation. Since it received US Food and Drug Administration approval in June 2003, the TIS has become 1 of the most widely used imaging systems in the United States. The benefits of the TIS, as noted in the literature, include the following: increased detection of and/or positive predictive value for high-grade squamous intraepithelial lesions (HSIL), an increase in productivity, and a decrease in the false-negative rate.[1-11]

Another important technological addition to cervical cancer screening is human papillomavirus (HPV) testing. HPV reflex testing of atypical squamous cells (ASC) of undetermined significance (ASC-US) cases has allowed for better identification of those women who should undergo colposcopy and biopsy versus those who can return to screening. This has resulted in overall decreased cost of cervical cancer screening and has helped to eliminate the over-treatment of patients in this population. More recently, it has been suggested that HPV testing may have a role in cytology quality-assurance practices.[12-16] According to the available literature, an appropriate percentage of high-risk HPV (HR-HPV)-positive ASC-US cases is approximately 40% to 50%.[15-17] By using the percentage of HPV-positive cases with the ASC to squamous intraepithelial lesion (ASC:SIL) ratio, a more accurate reflection of a cytotechnologist's or a laboratory's performance may be ascertained.[13] However, the manner in which implementation of the TIS influences ASC rates, ASC:SIL ratios and HR-HPV results has not been consistent between institutions.[1-11,14]

The objective of this study was to evaluate the effects of implementing the TIS at Brooke Army Medical Center (BAMC), a tertiary military medical center. Specifically, the following objectives were assessed: 1) whether the detection of squamous abnormalities was increased with the TIS, 2) how the rate of HR-HPV detection in ASC-US cases changed (or did not change) before and after putting the TIS into operation, and 3) how the TIS influenced productivity.

MATERIALS AND METHODS

Our laboratory processes and evaluates >50,000 ThinPrep Pap tests per year that originate from our institution and from 12 other, smaller military facilities. All slides are prepared using the ThinPrep 3000 processor (Hologic Corporation [previously Cytyc Corporation], Marlborough, Mass) according to the manufacturer's instructions, and are Pap stained. The Bethesda System 2001 terminology is used for all reports. HR-HPV testing is performed by the BAMC Microbiology Section using Digene Hybrid Capture 2 technology (Qiagen Inc., Valencia, Calif) according to the manufacturer's instructions. HR-HPV testing is ordered as a reflex test for cases that are signed out as ASC-US, and the HR-HPV results are unknown to the pathologist at the time the Pap test is signed out. The TIS was introduced into our laboratory in 2006. All cytotechnologists received 2 days of TIS training. Validation of the imager was performed in January 2006, and the TIS was put into routine use in February 2006. Of note, we had introduced the Imager Pap stain

Table 1. Cytologic Diagnoses Before and After ThinPrep Imaging System Implementation

Diagnosis	Historic Manual Screening, 2005	Imager-Detected Cases, 2006	2004 Probability, %	2005 95% CI Low	2005 95% CI High	2006 Probability, %	2006 95% CI Low	2006 95% CI High	Significant?
Total Pap tests	54,438	53,209							
NILM	49,585	47,858	91.1	.908	.913	89.9	.897	.902	Yes
ASC-US	2146	2007	3.9	.038	.041	3.8	.036	.039	No
ASC-H	117	258	.2	.002	.003	.5	.004	.005	Yes
AGC	14	29	0	.000	.000	.1	.000	.001	Yes
LSIL	1412	2067	2.6	.025	.027	3.9	.037	.040	Yes
HSIL	132	205	.2	.002	.003	.4	.003	.004	Yes
SCC	4	0	0	.000	.000	0	.000	.000	Indeterminate
AIS/ADCA	1	2	0	.000	.000	0	.000	.000	Indeterminate
UNSAT	1027	783	1.9	.018	.020	1.5	.014	.016	Yes

95% CI indicates 95% confidence interval; Pap, Papanicolaou; NILM, negative for intraepithelial lesion or malignancy; ASC-US, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells, cannot rule out high-grade squamous intraepithelial lesion; AGC, atypical glandular cells; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; SCC, squamous cell carcinoma; AIS, adenocarcinoma in situ; ADCA, adenocarcinoma; UNSAT, unsatisfactory.

protocol in a gradual fashion over the 6 months before implementation of the Imager.

The Anatomic Pathology Laboratory Information System (APLIS) of BAMC was queried for all Pap tests for the periods from February 2005 to December 2005 (manual screening) and from February 2006 to December 2006 (imager-assisted screening). The Clinical Pathology Laboratory Information System of BAMC was queried for HR-HPV results for all Pap tests that resulted in an ASC-US finding during the indicated periods. HR-HPV results were classified as positive, negative, or quantity not sufficient (QNS) for each test.

The APLIS of BAMC also was queried for all histology follow-up up to 1 year (including cervical biopsies, endocervical curettings, loop electrocautery excision procedures, cold knife cones, and hysterectomy specimens) after the Pap tests for the periods from February 2005 to December 2005 (manual screening) and from February 2006 to December 2006 (imager-assisted screening) were performed. The most severe histologic diagnosis made within 1 year of the index Pap test was considered the follow-up histologic diagnosis. Most of our referring facilities for Pap tests perform their own histology or refer their patients to civilian healthcare facilities for follow-up; thus, the amount of histology follow-up available for review was limited.

This was a retrospective observational study. The independent variable was time (2005, manual screening; 2006, imager-assisted screening). The dependent variable was the distribution of diagnoses of Pap tests. The null hypothesis was that there was no difference in the distribution of diagnoses between 2005 and 2006. The alternative hypothesis was that there was a difference in the distribution of diagnoses between 2005 and 2006. Because of the number of categories, the most efficient statistical test was a comparison of the probabilities of each diagnosis between years. The 95% confidence intervals (95% CI) for each diagnosis were calculated using the Wald equation. The histology results before and after TIS implementation were compared using the chi-square goodness-of-fit test. Productivity was calculated as the change in average slides screened per hour before and after the imager.

RESULTS

In total, 107,647 Pap tests were analyzed in the 2005 (54,438) and 2006 (53,209) timeframes, respectively. Table 1 shows detection rates of general cytologic diagnoses and rates of unsatisfactory cases for each timeframe. There is a statistically significant difference between 2 probabilities if neither probability falls within the 95% CI of the

Table 2. High-Risk Human Papillomavirus Results for Cases With Atypical Squamous Cells of Undetermined Significance Before and After ThinPrep Imaging System Implementation

Diagnosis	Historic Manual Screening, 2005	Imager-Detected Cases, 2006	2005 Probability, %	2005 95% CI Low	2005 95% CI High	2006 Probability, %	2006 95% CI Low	2006 95% CI High	Significant?
ASC-US	2145*	2007							
HR-HPV positive	1192	953	2.2	.021	.023	1.8	.017	.019	Yes
HR-HPV negative	871	974	1.6	.015	.017	1.8	.017	.019	Yes
ASC-US, QNS	82	80	.2	.001	.002	.2	.001	.002	No

95% CI indicates 95% confidence interval; ASC-US, atypical squamous cells of undetermined significance; HR-HPV, high-risk human papillomavirus; QNS, quantity not sufficient.
*One case of ASC-US was not forwarded for HR-HPV testing.

Table 3. Available Histology Follow-Up for the Period From February 2005 to December 2005

Cytologic Diagnosis	No. With Negative/Reactive Changes (%)	Histologic Follow-Up: No. Atypical/ Indeterminate for Dysplasia or HPV Cytopathic Effect (%)	LSIL: HPV Cytopathic Effect, CIN-1, or Mild Dysplasia (%)	HSIL or Greater: CIN-2 or CIN-3, Moderate to Severe Dysplasia, or SCC (%)	Total No. of Pap Tests With Histology (%)
ASC-US					
HR-HPV positive	49/209 (23.4)	28/209 (13.4)	99/209 (47.4)	33/209 (15)	209/1192 (17.5)
HR-HPV negative	45/83 (54.2)	5/83 (6)	32/83 (38.6)	1/83 (1.2)	83/871 (9.5)
ASC-H	9/46 (19.5)	2/46 (4.3)	14/46 (30.5)	21/46 (45.7)	46/117 (39.3)
LSIL	68/315 (21.6)	33/315 (10.5)	170/315 (54)	44/315 (13.9)	315/1412 (22.3)
HSIL	4/53 (7.5)	3/53 (5.7)	14/53 (26.4)	32/53 (60.4)	53/132 (40.2)

HPV indicates human papillomavirus; LSIL, low-grade squamous intraepithelial lesion; CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; SCC, squamous cell carcinoma; Pap, Papanicolaou; ASC-US, atypical squamous cells of undetermined significance, HR-HPV, high-risk human papillomavirus; ASC-H, atypical squamous cells, cannot rule out high-grade squamous intraepithelial lesion.

other. There were statistically significant differences in the distributions of all diagnoses between the years 2005 and 2006 except for ASC-US, squamous cell carcinoma (SCC), and adenocarcinoma in situ/adenocarcinoma (AIS/ADCA). SCC and AIS/ADCA were indeterminate, because use of the Wald equation requires that there be at least 10 observations in each arm of the distribution. With the TIS, detection rates of ASC cannot rule out HSIL (ASC-H), atypical glandular cells (AGC), low-grade SIL (LSIL), and HSIL increased significantly; whereas the rates of negative for intraepithelial lesion or malignancy (NILM) and unsatisfactory decreased significantly. Given the changes in detection rates of squamous abnormalities, as expected, the ASC:SIL ratio decreased significantly with the TIS from 1.5 to 1.0. The decreased ASC:SIL ratio was predominantly because of the increased detection of LSIL and HSIL.

Table 2 shows the HR-HPV testing results for the cases that were diagnosed as ASC-US with and without the TIS. One case of ASC-US was not forwarded for HR-HPV testing in 2005. The decrease in the ASC-US HR-HPV-positive proportion and the increase in the ASC-US HR-HPV-negative proportion after implementation of the TIS were statistically significant. The decrease in the proportion of ASC-US HR-HPV-QNS cases after implementation of the TIS was not statistically significant.

Tables 3 and 4 show the available histologic follow-up results for the 2005 and 2006 periods, respectively. For the cytologic diagnoses of ASC-US and ASC-H, the number of confirmed cases of SIL decreased, whereas the number of cases with negative follow-up increased. The histologic follow-up of LSIL Pap tests was very similar before and after implementation of the TIS. For HSIL Pap tests, the number of cases with negative results,

Table 4. Available Histology Follow-Up for the Period From February 2006 to December 2006

	Histologic Follow-Up				
Cytologic Diagnosis	No. With Negative/Reactive Changes (%)	No. Atypical/ Indeterminate for Dysplasia or HPV Cytopathic Effect (%)	LSIL: HPV Cytopathic Effect, CIN-1, or Mild Dysplasia (%)	HSIL or Greater: CIN-2 or CIN-3, Moderate to Severe Dysplasia, or SCC (%)	Total No. of Pap Tests With Histology (%)
ASC-US					
HR-HPV positive	14/110 (12.7)	20/110 (18.2)	57/110 (51.8)	19/110 (17.3)	110/953 (11.5)
HR-HPV negative	62/72 (86.1)	1/72 (1.4)	9/72 (12.5)	0/72 (0)	72/974 (7.4)
ASC-H	16/56 (28.6)	5/56 (8.9)	16/56 (28.6)	19/56 (33.9)	56/258 (21.7)
LSIL	95/398 (23.9)	37/398 (9.3)	220/398 (55.3)	46/398 (11.5)	398/2067 (19.3)
HSIL	2/82 (2.4)	2/82 (2.4)	13/82 (15.9)	65/82 (80.3)	82/205 (40)

HPV indicates human papillomavirus; LSIL, low-grade squamous intraepithelial lesion; CIN, cervical intraepithelial neoplasia; HSIL, high-grade squamous intraepithelial lesion; SCC, squamous cell carcinoma; Pap, Papanicolaou; ASC-US, atypical squamous cells of undetermined significance, HR-HPV, high-risk human papillomavirus; ASC-H, atypical squamous cells, cannot rule out high-grade squamous intraepithelial lesion.

atypical changes, and cervical intraepithelial neoplasia 1 (CIN-1) on histologic follow-up decreased, whereas the cases of histologically confirmed CIN-2 or greater increased. There was a statistically significant difference in the relation between cytology results and histology results between 2005 and 2006 ($P < .001$ with 15 degrees of freedom).

The average rate of slides evaluated per hour per cytotechnologist during the 2005 timeframe was 10 slides per hour versus 16 slides per hour during the 2006 timeframe. Use of the TIS in our laboratory resulted in a 60% increase in productivity.

DISCUSSION

Implementation of the TIS at BAMC significantly improved our unsatisfactory rate and increased our detection of ASC-H, AGC, LSIL, and HSIL and had no effect on our overall rate of ASC-US cases. Consequently, use of the TIS lead to a decrease in the ASC:SIL ratio. Although the overall rate of ASC-US did not change, the proportion of HR-HPV-positive ASC-US cases decreased significantly. To our knowledge, no other study that evaluated the effects of TIS implementation in their laboratory had this combination of changes in their quality-assurance statistics.

Biscotti et al[3] reported an increased in the detection of squamous abnormalities at the level of ASC-US or worse, but not LSIL/HSIL or worse, and a decrease in unsatisfactory cases. Chivukula et al[4] reported increased detection rates of LSIL and HSIL and a decrease in ASC-US cases with the TIS (no *P* values were provided). Davey et al[5] noted a decrease in unsatisfactory cases and an increase in the detection of HSIL. Pacheco et al[8] reported an increase in the detection of HSIL with the TIS and an increase in productivity by an average of 2.2 slides per hour. Schledermann et al[11] observed a decrease in unsatisfactory cases and a 42% increase in productivity with use of the TIS; however, unlike most studies, those authors observed a decrease in the rates of squamous abnormalities after TIS implementation. Roberts et al[10] observed no improvement in sensitivity or positive predictive value with the imager versus manual screening of ThinPrep slides, although sensitivity with the imager was superior to manual screening of conventional Pap slides. In this study, productivity improved significantly with the TIS versus manual screening of ThinPrep slides. None of the studies mentioned above considered HR-HPV results.

Lozano[2] reported the increased detection of ASC-US, LSIL, and HSIL and, thus, had no significant change in the ASC:SIL ratio. Similar to our study, they noted a decrease in the HPV-positive proportion of ASC-US cases. Dziura et al,[6] similar to Lozano, also reported increased detection rates of ASC-US, LSIL, and HSIL without a change in the ASC:SIL ratio and a decrease in HPV-positive ASC-US and ASC-H cases. Although Miller et al[7] observed an increase in LSIL and HSIL, their ASC-US rate decreased with an increase in the HPV-positive proportion. Papillo et al[9] observed an increase in all squamous abnormalities (including ASC-US, ASC-H, LSIL, and HSIL) with no significant change in the ASC:SIL ratio. Although their overall rate of ASC-US

increased, the HPV-positive proportion decreased by 17%. Finally, Thrall et al[14] observed no significant difference in their ASC-US cases after the TIS, and their HPV-positive proportion did not change. This study was different from the others, in that their laboratory specifically worked toward an objective of 50% HPV-positive ASC-US cases as a quality-assurance measure.

It has been suggested by some authors that the rate of HPV-positive ASC-US cases can be used as a quality-assurance indicator in gynecologic cytology.[12-16] An appropriate percentage of HPV-positive ASC-US cases seems to be approximately 40% to 50%.[15-17] Ko et al[13] demonstrated that, by using both the percentage of HPV-positive cases and the ASC:SIL ratio, a more accurate reflection of a cytotechnologist's or a laboratory's performance may be ascertained. The percentage of HPV-positive ASC-US cases may help reveal problems that are not necessarily obvious from the ASC:SIL ratio alone. For example, a decreased HR-HPV-positive rate with an appropriate ASC:SIL ratio may indicate overcalling of both ASC-US and SIL. Another example might be a situation in which the HR-HPV-positive rate is within the appropriate range and the ASC:SIL ratio is increased, which may indicate under calling of SIL. Thrall et al[14] suggested that, by using a benchmark of a 50% HR-HPV-positive ASC-US rate, they were able to maintain a stable ASC-US rate regardless of the screening method (ie, manual vs imager directed). Tworek et al[15] performed a College of American Pathologists (CAP) Q-probes study of 68 institutions and reported a 41% to 51% HR-HPV-positive ASC-US rate, similar to the ASC/LSIL Triage Study results (HR-HPV-positive rate, 48.9%)[17] and the results reported by Zuna et al[16] (average HR-HPV-positive rate, 43.7%). Those authors also suggested that performance beyond 2 standard deviations of the mean (44% in their Q-probes study) should prompt reassessment of a cytotechnologist's and/or a laboratory's diagnostic processes in evaluating Pap tests.

However, studies of how implementation of the TIS influences ASC rates, ASC:SIL ratios, and HR-HPV results have produced inconsistent results.[1-11,14] In our laboratory, we have never tried to maintain a particular HR-HPV-positive ASC-US rate, nor have we used it as a standard quality indicator. During the 2005 timeframe (manual screening), we noted an ASC:SIL ratio of 1.5 (50th percentile according to CAP quality standards)[18] with an HR-HPV-positive ASC-US rate of 55.6% (1192 of 2145 cases), which is slightly above the ideal range of 40% to 50%. This suggests that we were slightly under calling SIL before implementation of the TIS. After TIS implementation, we noted an "improvement" in our HR-HPV-positive ASC-US rate (47.5%; 953 of 2007 cases) with a decrease in our ASC:SIL ratio (below the 25th percentile according to CAP quality standards).[18] These statistics are more challenging to interpret. The ASC:SIL ratio decrease is appropriate because of the increase in detection of SIL with the TIS and because there was no significant change in the overall ASC-US rate. However, assuming that our patient populations were relatively stable regarding incidence of disease from 2005 to 2006, these numbers actually suggest that we may have been overcalling ASC-US cases (ie, under calling NILM cases) after implementation of the TIS. Because a greater percentage of our ASC-US cases were HPV-negative after we implemented the TIS, this suggests that at least some of the cases we were overcalling were clinically "insignificant" (ie, HR-HPV-negative ASC-US). Despite this possible overcall, because of the HR-HPV triage testing, the percentage of ASC-US patients referred to colposcopy (HR-HPV positive) actually decreased, from 2.2% to 1.8% after implementation of the TIS.

The increase in proportion of confirmed CIN-2 or greater with an HSIL Pap after implementation of the TIS in out laboratory suggests that our increased detection of HSIL Pap tests was "clinically significant." There was an increase in negative histologic follow-up with ASC-US and ASC-H Pap tests. In addition, a greater proportion of cases with negative or reactive findings on histology were ASC-US HR-HPV-negative after TIS implementation. Both of these findings further support the possibility that, after putting the TIS into use, we may have been overcalling "clinically insignificant" atypical Pap cases.

In the current study, the TIS had no significant impact on the ASC-US rate; whereas the HR-HPV-positive proportion of ASC-US Pap tests decreased, and the proportion of patients with negative histologic follow-up increased. We suggest that, at least initially, the use of imager-directed screening may increase the number of "clinically insignificant" ASC-US Pap tests. Because we introduced the Imager Pap stain protocol gradually, we attribute this change more to the types of cells the imager selects versus those noted during manual screening by a

cytotechnologist. The TIS seems to be more sensitive in the cells it selects over manual screening by the cytotechnologist alone. Using the TIS, we also noted a statistically significant increase of histology confirmed cases of HSIL Pap tests. In addition to the increased detection of HSIL, the main advantages we noted with TIS implementation were decreased unsatisfactory Pap tests (statistically significant) and a 60% increase in productivity. Overall, we were extremely satisfied with the implementation of the TIS in our laboratory. Further investigations will be necessary to determine whether the pattern noted here, most specifically the possible overcall of atypical Pap tests, has continued with routine use of the TIS and how these findings relate to the colposcopy/biopsy follow-up for these patients.

Conflict of Interest Disclosures

The authors made no disclosures.

References

1. Dawson AE. Can we change the way we screen? The ThinPrep Imaging System. Clinical trial data and early experience. *Cancer*. 2004;102:340-344.
2. Lozano R. Comparison of computer-assisted and manual screening of cervical cytology. *Gynecol Oncol*. 2007;104: 134-138.
3. Biscotti CV, Dawson AE, Dziura B, et al. Assisted primary screening using the automated ThinPrep Imaging System. *Am J Clin Pathol*. 2005;123:281-287.
4. Chivukula M, Saad RS, Elishaev E, White S, Mauser N, Dabbs DJ. Introduction of the ThinPrep Imaging System (TIS): experience in a high-volume academic practice [serial online]. *CytoJournal*. 2007;4:6.
5. Davey E, d'Assuncao J, Irwig L, et al. Accuracy of reading liquid based cytology slides using the ThinPrep Imager compared with conventional cytology: prospective study [serial online]. *BMJ*. 2007;335:31.
6. Dziura B, Quinn S, Richard K. Performance of an imaging system vs. manual screening in the detection of squamous intraepithelial lesions of the uterine cervix. *Acta Cytol*. 2006;50:309-311.
7. Miller FS, Nagel LE, Kenny-Moynihan MB. Implementation of the ThinPrep Imaging System in a high-volume metropolitan laboratory. *Diagn Cytopathol*. 2007;35:213-217.
8. Pacheco MC, Conley RC, Pennington DW, Bishop JW. Concordance between original screening and final diagnosis using imager vs. manual screen of cervical liquid-based cytology slides. *Acta Cytol*. 2008;52:575-578.
9. Papillo JL, St John TL, Leiman G. Effectiveness of the ThinPrep Imaging System: clinical experience in a low risk screening population. *Diagn Cytopathol*. 2008;36:155-160.
10. Roberts JM, Thurloe JK, Bowditch RC, et al. A 3-armed trial of the ThinPrep Imaging System. *Diagn Cytopathol*. 2007;35:96-102.
11. Schledermann D, Hyldebrandt T, Ejersbo D, Hoelund B. Automated screening versus manual screening: a comparison of the ThinPrep Imaging System and manual screening in a time study. *Diagn Cytopathol*. 2007;35:348-352.
12. Geisinger KR, Vrbin C, Grzybicki DM, Wagner P, Garvin AJ, Raab SS. Interobserver variability in human papillomavirus test results in cervicovaginal cytologic specimens interpreted as atypical squamous cells. *Am J Clin Pathol*. 2007;128:1010-1014.
13. Ko V, Nanji S, Tambouret RH, Wilbur DC. Testing for HPV as an objective measure for quality assurance in gynecologic cytology: positive rates in equivocal and abnormal specimens and comparison with the ASCUS to SIL ratio. *Cancer*. 2007;111:67-73.
14. Thrall MJ, Russell DK, Bonfiglio T, Hoda RS. Use of the ThinPrep Imaging System does not alter the frequency of interpreting Papanicolaou tests as atypical squamous cells of undetermined significance. *CytoJournal*. 2008;5:10.
15. Tworek JA, Jones BA, Raab S, Clary KM, Walsh MK. The value of monitoring human papillomavirus DNA results for Papanicolaou tests interpreted as atypical squamous cells of undetermined significance: a College of American Pathologists Q-probes study of 68 institutions. *Arch Pathol Lab Med*. 2007;131:1525-1532.
16. Zuna RE, Moore W, Dunn ST. HPV DNA testing of the residual sample of liquid-based Pap test: utility as a quality assurance monitor. *Mod Pathol*. 2001;14:147-151.
17. Solomon D, Schiffman M, Tarone R; for the ALTS Group.Comparison of 3 management strategies for patients with atypical squamous cells of undetermined significance: baseline results from a randomized trial. *J Natl Cancer Inst*. 2001;93:293-299.
18. College of American Pathologists.Cytopathology Checklist, September 27, 2007 ed. Northfield, Ill:College of American Pathologists; 2007.