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CytoProcessor™: A New Cervical Cancer Screening System for Remote Diagnosis

Elizabeth Faris Crowell[a] Cyril Bazin[a] François Saunier[b] Romain Brixtel[a] Yann Caillot[a] Boris Lesner[a] Matthieu Toutain[a] Carole Ferreri[c] Incarnation Garcia[c] Marie-Claire Mathieu[c] Jérôme Vaussanvin[c] Joëlle Depardon[c] Arnaud Renouf[a]

[a]DATEXIM, Caen, France; [b]SOFOS, Charbonnières-les-Bains, France; [c]Technipath, Limonest, France

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Digital pathology · Artificial intelligence · Cervical screening · Papanicolaou test · Gynecologic cytology

Abstract
Background: Current automated cervical cytology screening systems still heavily depend on manipulation of glass slides. We developed a new system called CytoProcessor™ (DATEXIM, Caen, France), which increases sensitivity and takes advantage of virtual slide technology to simplify the workflow and save worker time. We used an approach based on artificial intelligence to identify abnormal cells among the tens of thousands in a cervical preparation. ***Objectives:*** We set out to compare the diagnostic sensitivity and specificity of CytoProcessor™ and the ThinPrep Imaging System (HOLOGIC, Marlborough, MA, USA). ***Methods:*** A representative population of 1,352 cases was selected from the routine workflow in a private laboratory. Diagnoses were established using the ThinPrep Imaging System and CytoProcessor™. All discordances were resolved by a consensus committee. ***Results:*** Compared to the ThinPrep Imaging System, CytoProcessor™ significantly improves diagnostic sensitivity without compromising specificity. The sensitivity of detection of "atypical squamous cells of undetermined significance (ASC-US) and more severe" and "low-grade squamous intraepithelial lesion and more severe" was significantly higher using CytoProcessor™. Considering that cases with a truth diagnosis of ASC-US or more severe required clinical follow-up, 1.5% of the cases (21/1,360) would have been missed if the CytoProcessor™ diagnosis had been used for clinical decision-making. In contrast, 4% of the cases (54/1,360) were missed when the ThinPrep Imaging System diagnosis was used for clinical decision-making. There were 2.6 times fewer false negatives using CytoProcessor™. The CytoProcessor™ workflow was 1.5 times faster in terms of worker time. ***Conclusions:*** CytoProcessor™ is the first of a new generation of automated screening systems, demonstrating improved sensitivity and yielding significant gains in processing time. In addition, the fully digital nature of slide presentation in CytoProcessor™ allows the remote diagnosis of Papanicolaou tests for the first time.

Introduction

Cervical cancer remains the fourth most frequent cancer among women worldwide [1]. Only a decade after the Papanicolaou test had become widely accepted, as early

KARGER

E-Mail karger@karger.com
www.karger.com/acy

Elizabeth Faris Crowell
DATEXIM
51 avenue de la côte de nacre
FR–14000 Caen (France)
E-Mail research@datexim.com

as the 1950s, researchers recognized the potential to automate Papanicolaou screening [2]. However, the failure to reject false positives led to the abandonment of many early projects. It was discovered that basing decisions on one or a few parameters such as nucleus size or DNA content was insufficient, since such approaches failed to distinguish between debris and true cells, as well as between inflammation and true abnormality [2].

In spite of these difficulties, two automated screening systems have reached the market and attained considerable success [3]. These automated screening systems are direct descendants of technology from the 1980s, namely, AutoPap, now called the BD FocalPoint Slide Profiler (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), and PAPNET, renamed as the ThinPrep Imaging System (TIS; HOLOGIC, Marlborough, MA, USA) [2]. Since they were designed before the advent of rapid slide scanners and the possibility to fully digitize the workflow, these systems remain dependent on physical slides and a microscope.

In the case of the TIS, the screener places the slide on the microscope, and the system then positions the slide on the first selected field of view [3]. Once examined, the screener passes to the next field of view, until all 22 have been interpreted. If any suspicious cells are found, a full manual review must be conducted as required by the manufacturer.

The BD FocalPoint Slide Profiler works in much the same manner, but it has the added benefit of sorting slides into quantiles corresponding to the probability that the slide contains abnormalities [4]. The most interesting category is "no further review," which are slides that have a high probability of being normal such that no human interpretation is necessary. Studies have indeed confirmed that fewer than 1% of CIN2+ (cervical intraepithelial neoplasia grade 2+) cases would be designated as "no further review" in routine use [4–7].

Current automated screening systems select and present a fixed number of "fields of view" for each slide [3]. The same number of fields of view are selected whether the slide contains zero abnormal cells or hundreds of abnormal cells. The potentially abnormal cells are surrounded by a variable number of normal cells in the field. Thus, instead of screening the entire slide, the specialist must screen each field of view. Several clinical studies found that abnormal cells were often overlooked when presented in this fashion [4, 8, 9].

CytoProcessor™ (DATEXIM, Caen, France) is radically different from these other systems. The abnormal cells are presented individually (Fig. 1). This novel method of presentation is designed so that the screener does not miss an abnormal cell hidden among dozens of normal cells. There are no limitations to the number of cells presented in the gallery. If there are no abnormal cells detected on the slide, the gallery is empty, and the screener can move on to the next slide. If there are thousands of abnormal cells, they will all appear in the gallery, ordered by severity from high grade to low grade.

In this paper, we demonstrate the improved performance of CytoProcessor™ in terms of sensitivity compared to existing systems. We illustrate how virtual slide technology can offer laboratories significant gains in time by eliminating costly slide manipulation steps.

Materials and Methods

This single-center clinical study compared diagnoses established using the TIS with those established using CytoProcessor™.

Diagnostic Procedures

The HOLOGIC standard protocols were followed as recommended by the manufacturer to obtain the TIS diagnosis. If a suspicious cell was discovered in a field of view, the entire slide was manually screened. The screener's final diagnosis was used as the TIS diagnosis.

To reach the CytoProcessor™ diagnosis, a screener simply reviewed the first 100 cells selected by CytoProcessor™. No manual screening was made mandatory in any case. The screener could view the cells in the context of the slide if desired, by clicking on the cell in the gallery. No suggested diagnoses or metrics are provided by CytoProcessor™; the image alone is interpreted to reach a diagnosis.

The data presented in CytoProcessor™ were anonymized to blind the investigator to the original TIS diagnosis. The cases were presented in random order to the screeners, along with the clinical data. To reduce the effects of interobserver variability, cases were reassigned to the same investigator who had made the TIS diagnosis whenever possible (95% of the cases). A washout period of at least 3 weeks was respected to prevent the investigator from remembering the case.

The diagnoses were established using the Bethesda system, the internationally accepted guide for reporting diagnoses from cervical cytology [10]. The diagnostic categories are as follows for squamous cells, roughly in order of severity: negative for intraepithelial lesion or malignancy (NILM), atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion (HSIL) (ASC-H), HSIL, and squamous cell carcinoma. For glandular cells, they are as follows: atypical glandular cells (AGC); AGC, favor neoplastic (AGC neo); adenocarcinoma in situ (AIS); and adenocarcinoma (ADC).

Training

Nine investigators participated in the study, all of whom had at least 7 years of experience using the TIS. The investigators were

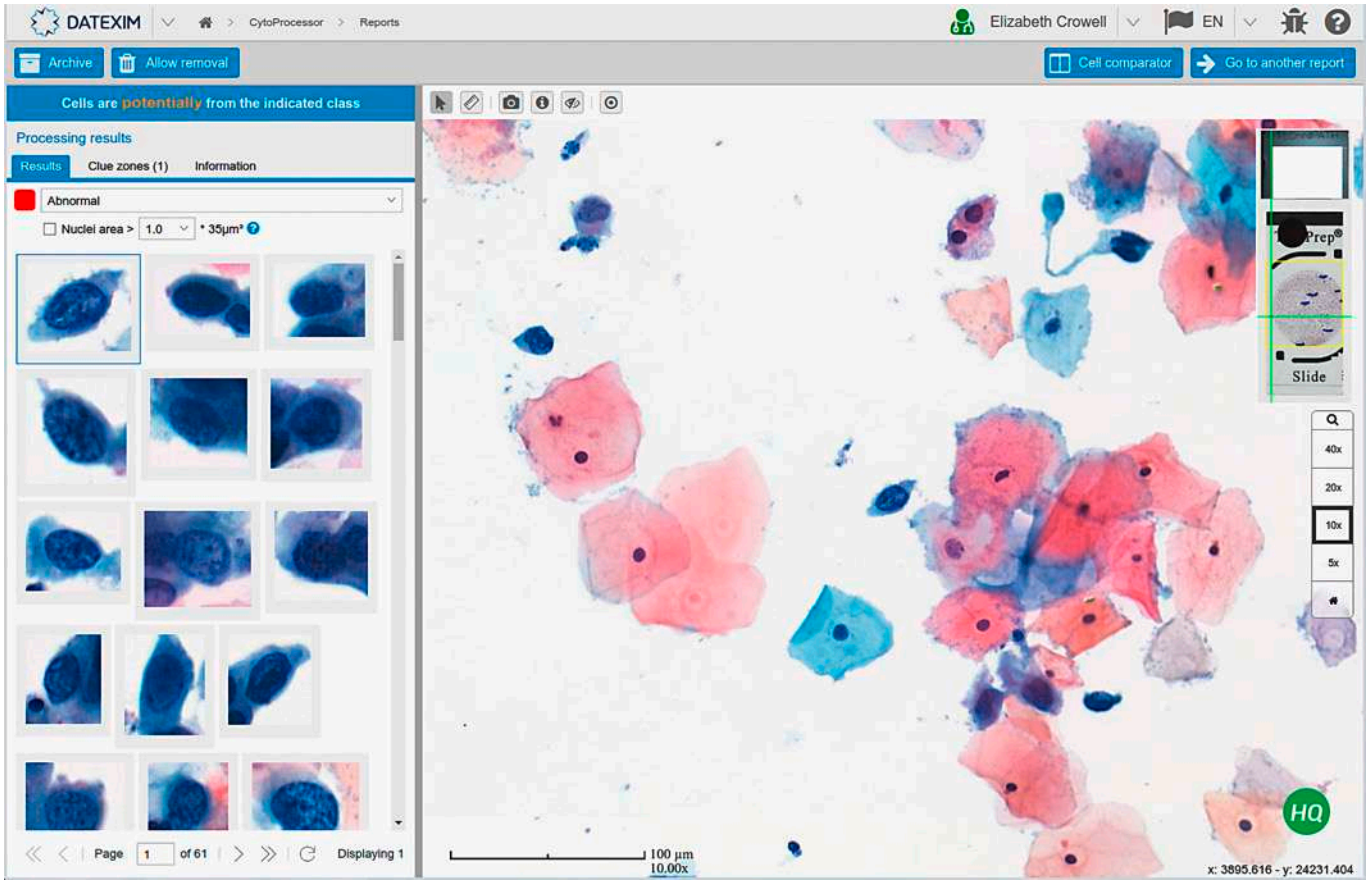

Fig. 1. The CytoProcessor™ user interface showing a gallery of abnormal cells.

given a 1-h training course in the use of CytoProcessor™ and 20 practice slides before beginning the study.

Determination of the Reference Truth Diagnosis

When the microscopic and CytoProcessor™ diagnoses were concordant, this was considered to be the truth diagnosis. Discordances were resolved by a consensus committee, blinded to the original diagnoses, and discussed until a consensus was agreed upon. The committee was composed of 7 investigators from the Technipath Laboratory (including authors C.F., I.G., and M.-C.M.). The consensus diagnosis served as the reference for all subsequent calculations of sensitivity and specificity. Out of 473 cases reviewed, no consensus was possible in 28 cases due to obscuring blood or low cellularity. These 28 cases were consequently excluded from the study.

Sample Preparation and Selection

All specimens were prepared using the ThinPrep technique and standard HOLOGIC protocols. Specimens for routine cervical cancer screening were collected after obtaining informed consent from the patients or their legal guardian. Only 1 patient did not consent to participate in the study. The slides were digitized at ×40 (resolution 0.28 µm/pixel) using a Pannoramic 250 slide scanner (3DHISTECH, Budapest, Hungary). No slides failed the scanning procedure. At onset, 9,186 TIS diagnoses were collected (9,123 for diagnosis and 63 for time measurements). Of these 9,186 cases, 6,026 met the inclusion criterion (patient 18 years or older). From this population, a random selection of 1,477 cases consisting of 59% NILM cases and 41% ASC-US or more severe was made for subsequent diagnosis with CytoProcessor™. Cases judged as unsatisfactory for analysis by either method were excluded. After these exclusions, this yielded a total of 1,352 cases, for which we obtained 1,360 diagnoses (8 cases were diagnosed twice).

In order to study the representativity of sample selection, clinical data were collected for all patients included in the study and for all patients screened between August 28, 2017, and January 5, 2018 (9,123 cases). We also investigated patient characteristics that can generate a specific gynecologic cytology result. The presence of an intrauterine contraceptive device is known to generate signs that can be misinterpreted as HPV infection. Pregnancy, postpartum repair, and breastfeeding also lead to specific observable changes. We compared the proportions of patients recorded as having received prior treatment for cervical lesions and verified that patients having had a hysterectomy were represented.

Statistical Analyses

Sensitivity was calculated as the number of true-positive diagnoses divided by the number of true positives plus false negatives,

Table 1. Proportions of diagnostic categories in the data set as determined using the original TIS diagnosis

Category	Cases, *n*	Percentage of total
NILM	802	59.00
ASC-US	192	14.00
LSIL	231	17.00
ASC-H	27	2.00
HSIL	87	6.00
Squamous cell carcinoma	0	0.00
AGC	9	0.70
AGC neo	2	0.10
AIS and ADC	2	0.10

TIS, ThinPrep Imaging System; NILM, negative for intraepithelial lesion or malignancy; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AGC, atypical glandular cells; AGC neo, atypical glandular cells, favor neoplastic; AIS, adenocarcinoma in situ; ADC, adenocarcinoma.

using the truth diagnosis as a reference. Specificity measures the proportion of correctly identified negatives among the total negatives as determined by the truth diagnosis.

Statistical significance was estimated by calculating confidence intervals and determining whether the intervals overlap. If the intervals did not overlap, the null hypothesis was rejected and it was concluded that a real difference existed. Confidence intervals were determined at 95% confidence by adding or subtracting

$$1.96\sqrt{\frac{\frac{P}{N}\left(1-\frac{P}{N}\right)}{N}}$$

from P/N, where P is the number of true positives detected and N is the number of true positives plus false negatives. If $N < 30$, Kauffmann's method was used to better estimate the intervals [11]. Other statistical tests were performed using R software version 3.2.3 GUI 1.66 Mavericks build (7060).

Results

Rejection Rate

1,477 cases were presented for diagnosis with CytoProcessor™. The investigator refused to provide a diagnosis in 125 cases, mostly due to the presence of obscuring blood (n = 110), low cellularity (n = 10), or severe inflammation (n = 3). These are all problems independent of CytoProcessor™ and caused by specimen preparation. In 3 of the 1,477 cases, the refusal to diagnose was due to a problem specific to the slide scanner, i.e., out-of-focus regions in the image. Overall, this yielded a rejection rate of 0.2%. This problem could likely have been resolved by rescanning the 3 slides.

Table 2. Proportions of patients recorded as having the characteristic in either population

Characteristic	Routine population	Study population
Intrauterine device	10.90%	10.30%
Prior treatment	3.10%	3.10%
Pregnant	1.20%	1.30%
Postpartum	0.30%	0.30%
Hysterectomy	0.80%	0.50%

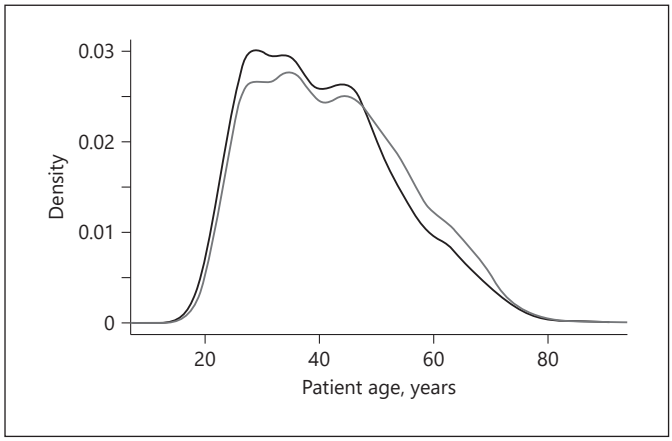

Fig. 2. Distribution of patient age at the time of screening for the study population (black) and the whole population screened between August 28, 2017, and January 5, 2018 (gray).

Number of Samples

There were 1,352 cases diagnosed by both methods (Table 1). Among these, 59% were NILM and 41% presented some degree of abnormality (ASC-US or more severe) according to the TIS diagnosis.

Representativity of the Data

The age distribution was nearly identical (Fig. 2); however, the proportion of patients aged 50 years and older was slightly underrepresented in the study population. This is most likely because the study population was enriched with abnormal cases, and patients 50 years and older less often present abnormalities. Every group showing a specific gynecologic cytology result was represented in the study at approximately the same proportion as in

Table 3. Sensitivity of detection of grouped Bethesda diagnostic categories comparing CytoProcessor™ and the TIS using the truth diagnosis as a reference

Bethesda category	Diagnoses, *n*	Sensitivity of the TIS (95% confidence interval)	Sensitivity of CytoProcessor™ (95% confidence interval)	Statistically significant
ASC-US+	509	0.89 (0.87–0.92)	0.96 (0.94–0.98)	Yes
LSIL+	325	0.89 (0.85–0.92)	0.95 (0.93–0.97)	Yes
ASC-H+	93	0.89 (0.83–0.96)	0.90 (0.84–0.96)	No
HSIL+	78	0.82 (0.74–0.91)	0.88 (0.80–0.95)	No
AGC+	4	1	1	No

Differences are determined to be statistically significant at 95% confidence if the intervals do not overlap. "AGC+" groups together all diagnoses of AGC, AGC neo, AIS, and ADC. TIS, ThinPrep Imaging System; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AGC, atypical glandular cells; AGC neo, atypical glandular cells, favor neoplastic; AIS, adenocarcinoma in situ; ADC, adenocarcinoma.

Table 4. Sensitivity of detection of specific Bethesda diagnostic categories comparing CytoProcessor™ and the TIS using the truth diagnosis as a reference

Bethesda category	Diagnoses, *n*	Sensitivity of the TIS (95% confidence interval)	Sensitivity of CytoProcessor™ (95% confidence interval)	Statistically significant
ASC-US	184	0.62 (0.56–0.69)	0.66 (0.59–0.73)	No
LSIL	232	0.80 (0.75–0.85)	0.88 (0.84–0.92)	No
ASC-H	15	0.73 (0.44–0.92)	0.80 (0.52–0.95)	No
HSIL	74	0.82 (0.74–0.91)	0.88 (0.80–0.95)	No
AGC+	4	1	1	No

Differences are determined to be statistically significant at 95% confidence if the intervals do not overlap. "AGC+" groups together all diagnoses of AGC, AGC neo, AIS, and ADC. TIS, ThinPrep Imaging System; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; AGC, atypical glandular cells; AGC neo, atypical glandular cells, favor neoplastic; AIS, adenocarcinoma in situ; ADC, adenocarcinoma.

the routine population (Table 2). We conclude that the study population was representative of the total population received at the study center.

Sensitivity

The TIS and CytoProcessor™ diagnoses were concordant in 936 out of 1,360 cases (69%). Since CytoProcessor™ is for use in screening, the most important goal is to successfully detect abnormalities of any category. Therefore, we first grouped together all cases having a truth diagnosis of ASC-US or higher (ASC-US+), LSIL or higher (LSIL+), ASC-H or higher (ASC-H+), and HSIL and cancer (HSIL+). All glandular abnormalities (from AGC to ADC) were grouped together, since there were only 4 cases with true glandular abnormalities.

CytoProcessor™ is superior to the TIS in the detection of all squamous lesions, and equivalent in the detection of glandular lesions (Table 3). The detection rates of ASC-US+ and LSIL+ are significantly higher at the 95% confidence level with CytoProcessor™ than with the TIS.

When each diagnostic category is considered individually, CytoProcessor™ again demonstrates a higher sensitivity of detection than the TIS (Table 4). Glandular lesions and adenocarcinoma were also successfully detected.

Table 5. Confusion matrices comparing CytoProcessor™ and the TIS

	Truth, *n*		
	Normal	Abnormal	Total
CytoProcessor™			
Normal	688	21	709
Abnormal	163	488	651
Total	851	509	1,360
TIS			
Normal	748	54	802
Abnormal	103	455	558
Total	851	509	1,360

Cases are determined to be "normal" (negative for intraepithelial lesion or malignancy) or "abnormal" (atypical squamous cells of undetermined significance or worse) using the truth diagnosis as a reference. TIS, ThinPrep Imaging System.

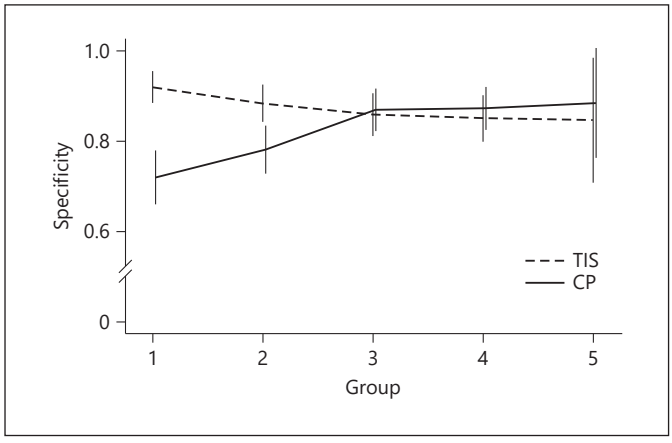

Fig. 3. Comparison of the specificity of CytoProcessor™ (CP; solid) with that of the ThinPrep Imaging System (TIS; dashed) over the course of the study. Each point represents groupings of approximately 40 cases of each investigator, ordered according to the time of diagnosis.

Table 5 shows the number of abnormalities detected when the cases were divided into "normal" and "abnormal" groups. If we consider these simplified groupings of normal and abnormal, we find that CytoProcessor™ yielded 1,176 correct diagnoses (86%) and the TIS gave 1,203 correct diagnoses (88%). Note that 163 out of 184 errors (89%) committed with CytoProcessor™ were "false positives," that is, normal cases diagnosed as abnormal (Table 5). This type of error occurred mainly at the beginning of the study (see Specificity below).

By examining the complete confusion matrix for CytoProcessor™ compared to the truth diagnosis (Table 6), we determined that the majority of errors were between the NILM and ASC-US groups. In contrast, the confusion matrix for the TIS compared to the truth diagnosis (Table 7) shows a wider variety of errors, including a greater number of false negatives for a similar number of false positives.

CytoProcessor™ made 21 false negative errors, whereas the TIS made 54 false negative errors (Table 5). Therefore, there were 2.6 times fewer false negatives when using CytoProcessor™. Considering the errors committed with CytoProcessor™, all represented less than 20% of the diagnoses in that category (Table 6). Overall, considering that cases with a truth diagnosis of ASC-US or more severe required clinical follow-up, 1.5% of the patients would have been missed if the CytoProcessor™ diagnosis had been used for clinical decision-making (21 out of 1,360). In contrast, 4% of the patients were missed when the TIS diagnosis was used for clinical decision-making.

Specificity

We observed a significant change in the specificity of CytoProcessor™ over the course of the study (Fig. 3). The investigators had 15 years of experience with the TIS and only a 1-h training period with CytoProcessor™. As can been seen in Figure 3, there was a noticeable learning curve before the investigators were able to efficiently reduce their rate of false positives. The specificity was relatively low at the beginning of the study (0.75; the first 540 diagnoses). In contrast, towards the end of the study (the last 325 diagnoses), the specificity of CytoProcessor™ had increased to 0.87. This was not significantly different from that of the TIS at 0.85 (Fig. 3).

Time to Diagnosis

Thus far we have illustrated that CytoProcessor™ performs better than the TIS in terms of diagnostic sensitivity. We next studied if this level of performance is achieved at the expense of time. To quantify the differences in total case processing time, we timed each step of the TIS workflow and the CytoProcessor™ workflow (see the online supplementary material; see www.karger.com/doi/10.1159/000497111 for all online suppl. material) and used data from a published study [12]. The extra time required to scan the slides in the CytoProcessor™ workflow is compensated by elimination of the slide handling and transfer steps. As can be observed in Table 8, the total workflow time is equivalent with the two methods when machine time is taken into account. In contrast, when only the steps requiring human inter-

Table 6. Confusion matrix for CytoProcessor™ diagnoses compared with truth diagnoses

	Truth						
	Normal	ASC-US	LSIL	ASC-H	HSIL	AGC+	Total
Normal	688	15	6	0	0	0	709
ASC-US	105	122	10	0	0	0	237
LSIL	40	34	204	0	9	0	287
ASC-H	9	5	1	12	0	0	27
HSIL	6	8	11	2	65	0	92
AGC+	3	0	0	1	0	4	8
Total	851	184	232	15	74	4	1,360

The diagonal represents diagnoses exactly matching the truth. ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. "AGC+" groups together all diagnoses of AGC, AGC neo, AIS, and ADC.

Table 7. Confusion matrix for ThinPrep Imaging System diagnoses compared with truth diagnoses

	Truth						
	Normal	ASC-US	LSIL	ASC-H	HSIL	AGC+	Total
Normal	748	39	14	1	0	0	802
ASC-US	55	115	20	0	2	0	192
LSIL	23	15	186	0	7	0	231
ASC-H	10	3	0	11	4	0	28
HSIL	7	11	12	3	61	0	94
AGC+	8	1	0	0	0	4	13
Total	851	184	232	15	74	4	1,360

The diagonal represents diagnoses exactly matching the truth. ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells – cannot exclude high-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. "AGC+" groups together all diagnoses of AGC, AGC neo, AIS, and ADC.

vention are considered, the CytoProcessor™ workflow is 1.5 times faster (Table 8).

If we assume that 5% of slides will be reviewed by a pathologist, we find that with every 100 slides the laboratory saves 2.2 h of worker time. For a working day of 6 h, this represents a time saving of 371 working days every 100,000 slides.

Table 8. Comparison of the total workflow time per slide between the TIS and CytoProcessor™

	TIS total time	CytoProcessor™ total time
Human + machine time	594 s/slide	595 s/slide
Human time only	436 s/slide	290 s/slide

The raw data are from online supplementary Table S1. "Human time only" represents total time minus machine time (steps in gray in online suppl. Table S1). TIS, ThinPrep Imaging System.

Discussion

CytoProcessor™ uses machine learning and multiparametric measurement of hundreds of cellular characteristics to successfully classify cells while excluding debris [13]. The slides are scanned automatically in batches of

up to 1,000, and the images are analyzed in the background by CytoProcessor™. Screeners can access the results and view the whole-slide image from anywhere using a simple web browser. In much the same way as the initial screener circles cells with a marker on the glass slide, the screener can mark pertinent cells in CytoProcessor™ with a single click of the mouse, highlighting them for secondary screeners and the pathologist.

In this study, we have demonstrated that CytoProcessor™ performs better than the TIS for screening of gynecologic cytology in a representative study population. The investigators achieved significantly higher sensitivity values using CytoProcessor™ than with the TIS. In our study, the risk of a false-negative diagnosis with CytoProcessor™ was remarkably low (1.5%), and statistically lower than that measured for the TIS (4%). In the context of the routine workflow, these performances were obtained with the added benefit of approximately 1.5 times faster slide processing.

Initially, the lower specificity of CytoProcessor™ may have been partly due to the different presentation of cells in CytoProcessor™ compared to the TIS. CytoProcessor™ presents a grouping of the most suspicious-looking cells on the slide, whereas the observer of a microscope slide sees a few suspicious cells surrounded by normal cells. With regular feedback on the first 100 slides, the investigators achieved a specificity equivalent to that with the TIS. CytoProcessor™ was found to be a robust system, performing better than the TIS regardless of individual variations due to the investigators, their experience, or the time of diagnosis.

The process failure rate, or percentage of runs for which no diagnosis could be made due to failure of the system, was 0.2%. All 3 failed runs were due to the image being out of focus. These problems could likely have been resolved by rescanning the slides. This process failure rate was severalfold lower than those reported for the TIS at 7.8% [14], 4.8% [15], and 3.99% [4].

Studies have shown that up to 60% of the total screening time is consumed by basic tasks such as slide handling, which require no specific training [12]. Screening represents a relatively incompressible step in total case processing. Time savings can be attained by concentrating essentially on other steps of the workflow. The novel digital slide system used in CytoProcessor™ makes it possible to eliminate the tedious slide handling tasks so that laboratories can save time. CytoProcessor™ is also scalable: accelerated processing rates can be obtained simply by adding more computing and scanning capacity to enable more slides to be analyzed in the same time frame.

Here, we demonstrated the performance of CytoProcessor™ on ThinPrep slides, but CytoProcessor™ has also been validated for diagnosis with slides prepared using the ILSA and NovaPrep slide preparation systems (unpublished data). CytoProcessor™ is adaptable to different liquid-based slide preparations, allowing laboratories to conserve their existing equipment. Implementation of CytoProcessor™ requires only the acquisition of computers to analyze the slides and view the results, and a slide scanner, which can additionally be used for other applications in the laboratory, such as transmitting histological images to collaborators.

Finally, the unique design of CytoProcessor™ allows the results to be accessed from anywhere using a web browser. Instead of placing the glass slide on a specialized microscope, the screener simply opens a web browser on any standard computer and connects to CytoProcessor™. This flexibility allows slide preparation to be centralized at one site, while screeners make their diagnoses from multiple, remote locations.

Using CytoProcessor™ as an aid for diagnosis resulted in a detection sensitivity superior to that of the TIS, for an equivalent specificity. Due to the time savings produced by the simplified CytoProcessor™ workflow, CytoProcessor™ additionally permits more slides to be processed without any increase in workforce. The use of virtual slide images greatly accelerates data transmission and avoids the risk of breaking fragile glass slides during transport. Together, these advantages represent a benefit for the laboratories, which can reduce costs, and likewise for the patients, who can obtain access to cervical cancer screening in resource-poor areas and reduce delays in diagnosis.

Acknowledgements

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Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki. All subjects who participated gave their informed consent. Before enrollment of the first patient, this study was declared to the French National Agency of Medicine and Health Products Safety (ANSM) under the reference No. 2017-A00212-51.

Disclosure Statement

The authors were paid standard wages by DATEXIM for their work on the study. No financial advantages or conflicting interests are disclosed.

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