Automated instruments or devices are common in many professions. The medical laboratory industry is no exception. The primary aim of automation in the laboratory is to allow the technologists time to perform the more technical and challenging tests that have not yet been automated and to check the accuracy of the results produced by the instruments.

Cytology laboratory personnel were resistant to automation initially; however, automation in the cytology laboratory is now a reality. The goals that automating the cytology laboratory seeks to achieve are:

- Improving the accuracy of test results
- Shortening the length of time needed to perform the tests
- Obtaining a slide that is representative of the original sample collected from the patient

The concept of a computer-assisted or automated cytology laboratory has been the dream of cytopathologists and cytotechnologists for many years. As early as 1951, attempts were made to automate cervical smear screening using the Cytoanalyzer (Airborne Instruments Laboratories, Mineola, NY). These attempts were soon abandoned owing to the complexity of the then-current computer programs and the imaging capability required to accurately prepare and screen a Papanicolaou (Pap) smear.1

The quest to combine computer technology and microscopy in the production of an automated Pap smear preparatory or screening device did not become a reality until 1995 when the AutoPap (Neopath, Redmond, WA) system was approved by the US Food and Drug Administration (FDA).2

The automated devices currently available for use in cytology laboratories can be placed into 3 broad categories:

1. Specimen collection and preparation devices
2. Manual screening adjunctive devices
3. Automated screening devices

**Specimen Collection and Preparation Devices**

The FDA has approved 2 automated systems for specimen collection and preparation: the ThinPrep Processor (Cytyc, Boxborough, MA) and the AutoCyte Prep (AutoCyte, Elon College, NC, now a part of TriPath Imaging, Burlington, NC). Both systems use fluid-based collection devices for the collection of the specimens. However, the 2 systems use totally different techniques for preparing monolayer slides.

**ABSTRACT**

Automation of laboratory medicine is a growing concept that has involved virtually every type of clinical laboratory testing. This article discusses the automated devices currently available for use in the cytology laboratory and the principles governing the action of these automated instruments. The instruments are grouped into 3 main categories: specimen collection and preparation devices, manual screening adjunctive devices, and automated screening devices.

From Quest Diagnostics, Metairie, LA.

Reprint requests to Ms Icho, PO Box 7521, Metairie, LA 70010.
ThinPrep Processor
The FDA approved the ThinPrep processor in May 1996.\(^3,4\) Samples are collected with a plastic collection vial; then they are rinsed in a PreservCyt solution. This solution, a methanol-based buffered solution, is designed to maximize the recovery of the diagnostic cells by lysing RBCs and preserving the collected epithelial cells during specimen transport to the laboratory.\(^3\) The dispersion step of the ThinPrep processor gently breaks up large clumps of cells, mucus, and debris, and thoroughly mixes the cell sample. The cell solution is then drawn through a filter by a vacuum pump gathering diagnostic cells on the filter surface while RBC fragments and debris pass through the filter. The filter is inverted onto a glass slide, which transfers the diagnostic cells to the slide. The ThinPrep processor enhances the diagnostic accuracy of the Pap smear by removing artifacts associated with air drying and areas of thick smear and blood to enhance specimen adequacy.\(^3,6-8\) Samples must be prepared 1 at a time, so this method may not be a viable alternative for big cytology laboratories. The preparation time for each slide varies from 15 to 35 minutes, depending on the cellularity of the sample.

AutoCyte Prep System
The AutoCyte Prep was developed to automate and optimize epithelial cell enrichment, cellular transfer, and the individual staining of the Pap smears.\(^9,10\) It was approved by the FDA for nongynecologic specimens in 1996.\(^11\) and for gynecologic specimens in June 1999. The sample is collected in a container that holds a liquid preservative (AutoCyte solution). In the laboratory, samples undergo a density gradient centrifugation to reduce debris and inflammatory cells.\(^9\) The sediment is then resuspended and placed in the AutoCyte instrument where it undergoes sedimentation onto a glass slide. The slides are fixed and stained individually by the machine. Unlike the ThinPrep, which processes 1 specimen at a time, the AutoCyte processor can process a batch of 48 samples in about 1 hour and 45 minutes.

Manual Screening Adjunctive Devices
A manual screening adjunctive device speeds up the manual screening process. It maps out specific fields on slides that the cytotecnologist needs to review as opposed to the technologist screening the entire slide.

The Pathfinder
The Pathfinder was developed by Compucyte (Boston), which was later purchased by Neopath, now a part of TriPath Imaging. The Pathfinder is considered an adjunctive screening device because slides are manually screened by cytotecnologists. It did not require FDA approval.\(^2\) The Pathfinder system is attached to a microscope stage with a bracket. It consists of a 5-in monitor, a keyboard, and a storage device. During the screening process, the Pathfinder maps the area of each smear that has been screened by the cytotecnologist, calculates the average percentage of fields overlapped, and records the time that the cytotecnologist spent evaluating the smear.\(^12-15\) The Pathfinder was not widely adopted by cytoology laboratories and is no longer manufactured or marketed.

Trac Cell 2000 System
The Trac Cell 2000 is manufactured by Accumed (Chicago) and is popularly known as the Accumed. In August 1997, the FDA approved the system for use with conventional cervical smears, and in October 1998, it was approved for use with ThinPrep liquid-based preparations.

The Accumed integrates DNA stains and analytical software with the computer-aided microscopy workstation. The system performs automated assays of cellular DNA and measures malignancy-associated changes, ie, subtle changes that take place in the nuclei of apparently normal cells found near cancer or precancerous tissue. Measurement of such changes can be used to increase the sensitivity of lung cancer detection at an early stage and the detection of other types of cancer and precancerous conditions.
Automated Screening Devices

Only 1 automated screening device approved by the FDA is currently available. A second device approved by the FDA is no longer available, while a third device is currently undergoing the FDA approval process.

The Papnet System

This automated screening device is designed to detect rare abnormal cells when present in a conventionally prepared slide. It was developed by Neuromedical Systems (Suffern, NY) and approved by the FDA in November 1995 for quality control purposes. It uses the principle of neural network processing, which emulates the pattern recognition and parallel-processing capabilities of the human brain.

In March 1999, Neuromedical Systems filed a chapter 11 bankruptcy petition in US Bankruptcy Court. The intellectual rights to the Papnet technology were purchased jointly by AutoCyte and Neopath (now TriPath Imaging) in May 1999. Neither of the companies is currently supporting, marketing, or otherwise using the existing Papnet systems.

The AutoPap 300 System

This primary screening system was developed by Neopath. The AutoPap automates the screening of conventionally prepared cervical smears. It is currently undergoing the FDA approval process for the screening of monolayer slides prepared with the AutoCyte Prep system. The AutoPap 300 was approved by the FDA as a quality control tool in 1995. In May 1998, it became the only system approved by the FDA for the primary screening of slides with the ability to release the results of 25% or less of all the slides screened by the instrument that were negative. In other words, a maximum of 25% of the total slides screened and found to be negative can be released without rescreening by a cytotechnologist. This reduces the number of slides a cytotechnologist has to screen.

The system uses the principle of image analysis algorithms to screen the slides. The AutoPap scans the slide, capturing images. The images are analyzed using 5 algorithms:

- Strip detection
- Focus check
- Single cell
- Group
- Thick group

The information obtained from the 5 algorithms is combined to calculate an evaluation score that represents the likelihood of an abnormality on a slide.

In the primary-screening mode, the instrument screens the slides and ranks them into 2 categories:

- Archive or no further review. These slides need no manual review and are signed out as negative. Only a maximum of 25% of the total slides loaded on the instrument at any particular time can be archived.
- Review required. These slides require screening by a cytotechnologist. They are placed into quintiles first to fifth, with those in the first quintile having a higher probability of containing abnormal cells and those in the fifth quintile having the least probability.

The AutoCyte Interactive System (AutoCyte Screen)

This automated screening system was developed by AutoCyte, now a part of TriPath Imaging. The AutoCyte is currently undergoing FDA clearance to be approved for the screening of monolayer cervical smears. It uses the same principle of algorithmic classifiers as does the AutoPap, presents a computer evaluation derived from the population histogram analysis, and allows the technologist to view specific fields on the slide and make the final decision.

Conclusion

Automation in cytology has taken a long time to be realized, but it is now a reality. Pressure by the public and by the manufacturers of these automated devices for laboratories to produce an accurate diagnosis with the Pap smear (100% sensitivity) has influenced many laboratories to purchase these devices. Despite their high cost, none has eliminated false-negative Pap results or the need for cytotechnologists.
Automated screening devices have been on the market for a relatively short period. It is premature to assess their impact on the improvement of the diagnostic accuracy of the Pap smear. The public and cytology laboratory professionals must give these systems some time before assessing the impact of automation on the field of cytology.  

References