The Cytopathology & Informatics Partnership:

Current and Future Roles of Informatics in Cytopathology

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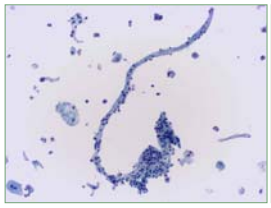
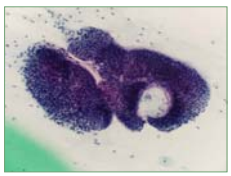
The Cytopathology & Informatics Partnership



Conflict of Interest

- **CAP Diagnostic Intelligence and Health Information Technology (DIHIT) Committee Member**
- **BioImagene Medical Advisory Board**



CURRENT STATE

- **Field of Cytopathology:**
  - Area of Anatomical Pathology most akin with Clinical Pathology.
  - High volume of specimens, repetitive tasks, & many standards.
- **Informatics advances:**
  1. Leveraging the Lab Information System (LIS).
  2. Standardized Diagnostic Criteria & Reporting.
  3. Adoption of Digital Imaging.
  4. Automation (computer-assisted screening).
  5. Ancillary Testing & Personalizing Medicine.

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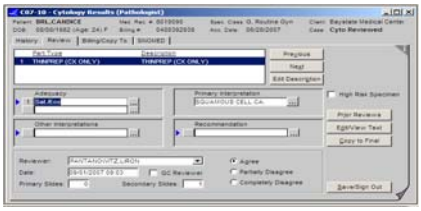
1. Leveraging the LIS

- **Lab Information System (LIS) at the core of most cytopathology lab operations.**
- **LIS functions include:**
  - Workflow management.
  - Data entry, Reporting, & Archiving.
  - Code capture & Billing.
  - Interfacing with other systems.
  - Assistance with regulatory compliance.

LIS View

Screenshot of a cytology-LIS showing its capabilities of connecting a fictitious patient's clinical history, workflow process in the laboratory, diagnostic interpretation (Review tab), billing, and coding (e.g. SNOMED).



LIS Test System

DATABASES

- **LIS represents a large complex electronic relational database.**
  - Relational database = multiple related tables linked via common shared files.
  - Ready for harvesting!
- **Benefits of electronic data include:**
  - Flexible & efficient way to store, retrieve & manipulate data.
  - Rapid transmission & exchange of data.
  - Integration of multiple databases.
  - Decreased storage space requirements.
  - Multiple user access to stored information.
- **Manipulation of extracted data (datasets) is feasible with spreadsheet applications, such as Excel.**

QC/QA Indicators

Purpose:

- **Help detect, correct, and reduce lab errors:** e.g. potential false negative Pap tests.
- **Meet regulatory requirements:** e.g. CLIA '88
- **Maintain accreditation:** e.g. CAP, Joint Commission.
- **Provides individual feedback & continuing education for staff.**

Process:

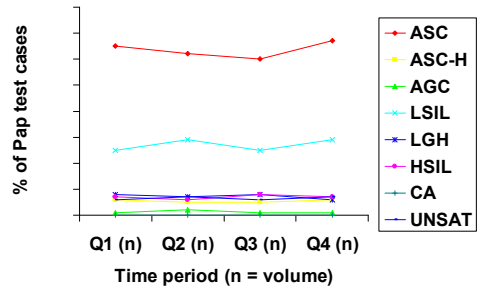
- **Quality of the overall testing process needs to be continuously monitored.**
- **Requires utilization of the LIS & electronic databases.**
- **Cross referencing of LIS data, comparison of findings against lab averages, and trend analyses.**

Screening & Performance Indicators

Pantanowitz et al. *Cytojournal*. 2008; 5:16.

- **Re-screening of random and high risk cases.**
- **5-year look back.**
- **Frequencies of diagnostic categories.** e.g. ASC-US/SIL rates.
- **HPV DNA positivity rates for ASC-US cases.**
- **Cytologic-histologic correlation.** e.g. Pap test & cervix biopsy.
- **Diagnosis correlation between cytotech & cytopathologists.**
- **Cytotechnologist reporting errors.**
- **Specimen turnaround time.**
- **Productivity (volume of slides/month).**

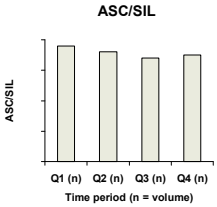
Diagnostic Categories

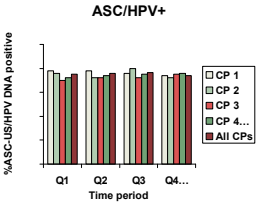


Fictitious data for presentation purposes

Old & New INDICATORS

Pantanowitz et al. *Diagn Cytopathol* 2009 Sep 30
Chhieng et al. *Diagn Cytopathol*. 2009; 37:320-3.





- **Greater utilization of hr-HPV data as a potential cytopathology lab QA indicator.**

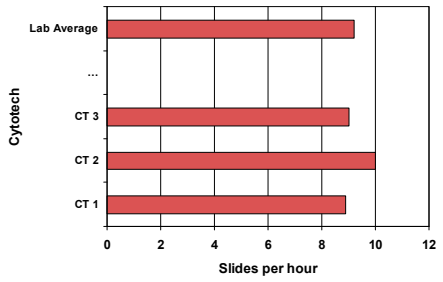
Fictitious data for presentation purposes

Cytologic/Histologic Correlation

Example of a contingency table

		Histologic Diagnosis						
Time period	Cytologic Diagnosis	NILM	ASC	AGC	LSIL	HSIL	CA	Grand Total
Q1	NILM							
	ASC							
	ASC-H							
	AGC							
	LSIL							
	LGH							
	HSIL							
	CA							
Q1 Total								
Q2	NILM							
	ASC							

Slides per Hour by Cytotechnologist

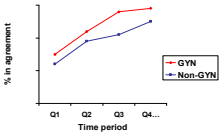


Fictitious data for presentation purposes

Additional Measures

- **Electronically alert providers of patients with a Pap test of HSIL or Cancer without documented follow up after a specific time period** (follow-up letters, autofax &/or via EMR inbox).
- **Generation of marketing and sales reports.** e.g. Turnaround time.
- **Tracking resident/fellow vs cytopathologist diagnoses.**

Henninger et al. *Cancer Cytopathology* 2008; 114:402-403.

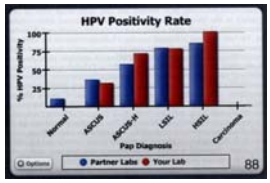


Fellow Diagnostic Agreement over Time
(fictitious data)

Web-site consortium

- Example: **Genetics Café** is an interactive web site to compare one lab's findings to cumulative group results.

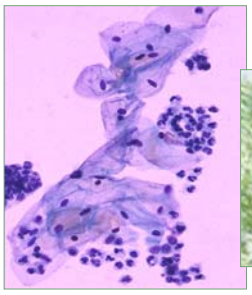
Howe & McGlennen. *Arch Pathol Lab Med* 2009; 133:1707.



CYTOLOGY LAB LEAN APPROACH

Raab et al. *AJCP* 2006; 126:585-92. Raab et al. *Am J Obstet Gynecol.* 2006; 194:57-64. *Dark Report* Nov 10, 2008.

- **Statistical QC is helpful for tasks in which numbers are generated.**
- **Application of the Toyota Production System process to GYN & Non-GYN Cytology may help identify and eliminate waste.**
- **Proven reduction in cytology diagnostic errors.**
- **Improved Papanicolaou test quality.**
- **Previously implemented initiatives:**
  - **Continuous pull system workflow process.**
  - **Adoption of a standardized diagnostic terminology scheme for thyroid FNA.**
  - **Immediate interpretation FNA service.**



2. STANDARDIZED REPORTING

- **Our core mission is to provide information in a manner most effective for patient care (i.e. for clinical decision support).**
  - Information must be accurate, timely, understandable, & available when needed.
- **Cervical cytology results were reported using various terminologies during the first 40 years of Pap test screening.**
  - Many labs modified reporting to suit there own needs.
  - Terms did not correspond to current knowledge of cervical carcinogenesis.
- **Challenge: Establish diagnostic criteria ↔ Standardize reporting ↔ Evaluate Outcomes.**

Papanicolaou's Classification

- 1943 "classes" introduced to describe pre-cancerous squamous lesions of the uterine cervix:

  Class I – Absence of atypical or abnormal cells
  Class II – Atypical cytology but no evidence of malignancy
  Class III – Cytology suggestive of but not conclusive for malignancy
  Class IV – Cytology strongly suggestive of malignancy
  Class V – Cytology conclusive for malignancy

The Bethesda System (TBS)

- A system for uniformly reporting cervical cytology was introduced in 1988, revised in 1991 & 2001.
- Adopted as the standard of reporting in USA by the Center for Disease Control & Prevention, the executors of CLIA 1988.
- Broad interdisciplinary participation in this consensus process.
- Diagnostic categories tied to rational evidence-based management algorithms (e.g. ASCCP) & outcomes.
- Followed by the recent Bethesda system diagnostic framework for reporting thyroid FNA results.

Davey DD. *Cancer J* 2003; 9:327-34. Solomon et al. *JAMA* 2002; 287:2114-9. Cibas & Ali. *Am J Clin Pathol* 2009; 132:655-7.

ADVANTAGES

- Conducive to rapid electronic sign out.
- Improves communication among cytologists, surgical pathologists & health care providers.
- Promotes clear management guidelines.
- Facilitates data extraction, exchange and analysis.
- Inspires multi-institutional studies.
- Offers a mechanism for modification & reform.
- An important component to improve cervical cancer screening.
- Ultimately improves patient care.

"Terms without Borders"

- Europe still has many different systems of cytology classification and languages.
- European guidelines being developed for different countries to adapt their terminology to make these screening programs comparable.
- British Society for Clinical Cytology (BSCC) closely aligned with TBS.

Herbert DA. *Diagn Cytopathol* 2005; 33:352-5.
Herbert et al. *Cytopathology* 2007; 18:213-9.

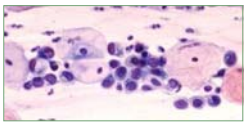
Bethesda Interobserver Reproducibility Study (BIRST)

Sherman et al. *Cancer Cytopathology* 2007; 111:15-25.

- Glass slides: Interobserver agreement for SIL on LBP is good & superior to conventional smears.

  Chhieng et al. *Cancer* 2002; 96:67-73.

- BIRST Web-based assessment of TBS (2001) for classifying cervical cytology:
  - 77 online images (broad range)
  - 216 Cytotechnologists & 185 Pathologists
  - Compared to TBS panel
  - 55.1% exact agreement
    - Highest for LSIL
    - Lowest for ASC-US or ASC-H
- Limited reproducibility of cervical cytologic interpretation.



Bethesda Interobserver Reproducibility Data:

NILM (negative for intraepithelial Lesion or Malignancy)		68	11%
Endometrial cells in a woman >= 40		14	2%
ASC-US		17	3%
ASC-H		108	17%
LSIL		3	0%
HSIL		324	52%
Invasive Squamous Cell Carcinoma		2	0%
Atypical Endocervical Cells		42	7%
Atypical Endometrial Cells		22	4%
Adenocarcinoma in situ (AIS)			
Endocervical		8	1%
Adenocarcinoma		12	2%

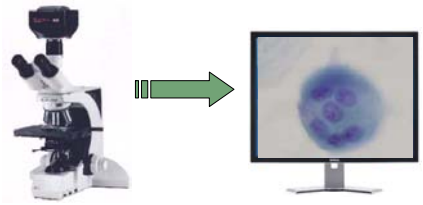
Can computer-assisted image analysis do a better job?

3. DIGITAL IMAGING

- Applications for Cytology:
  - Education & Research
  - Telecytology
  - Proficiency Testing
  - Automated Pap Screening
  - Pap Test Replacements
  - Other (e.g. QA/QC, image-enhanced reports, archiving, etc.)

TELECYTOLOGY

- Practice of cytology at a distance using telecommunication to transmit images.



Digital Workstation ↔ Network ↔ Remote Image Display

TELECYTOLOGY

- For diagnosis, consultation, conferences, QA review, & education.
- Static imaging (snap shot) involves the capture & sending of selected field of views.
- Robotic microscopy (real-time) uses a video camera, web conferencing &/or remotely operated microscope.
- Virtual microscopy uses images generated with whole slide scanning systems.
- Early efforts limited by computer power & software.
- Early studies were less accurate than light microscopy.
- However, more recent data demonstrate improved accuracy & reproducibility.
- Becoming useful for immediate assessment of FNA.

Telecytology Publications

Pantanowitz et al. *Cytojournal.* 2009; 6:6.

Date	Country	Specimen	System	Concordance (Image vs Slide)	Observer Agreement	Limitations
1996	USA	GYN	Static	60%	Fair	Frequent undercalling of dysplasia
1998	Germany	GYN	Dynamic*	65%	Not recorded	Monolayers more problematic than conventional smears
1998	USA	Non-GYN	Static	67-91%	Not recorded	Insufficient images and poor image quality
2000	USA	Non-GYN	Static	80-96%	Good	Inexperience with the system
2001	USA	GYN	Static	Good (no % recorded)	Moderate	Poor reproducibility
2001	USA	Non-GYN	Static	69%	Not recorded	Poor quality images (out of focus)
2003	USA	Non-GYN	Static	Good to excellent	Moderate	Poor quality images with inability to focus on thick cellular groups
2004	Japan	GYN & non-GYN	Static	89%	Not recorded	Lengthy time (up to 20 minutes) to capture images
2007	Iran	Non-GYN	Static	89%	Good	Lengthy time (up to 30 minutes) to capture images of poor quality

*Although a remotely controlled (dynamic) telecytology system was employed in this study, only preselected (static) areas were used.

PROFICIENCY TESTING

- Current gold standard is manual screening or review of glass slides.
- Virtual microscopy is being recommended by several investigators.
- CytoView = prototype computer image-based GYN cytology PT.
- Pros: Cost effective & improved standardization.
- Cons: Prior training is required, lengthy time to examine digital images, connectivity need, & this may not reflect the real-world experience.

Taylor et al. *Acta Cytol.* 1999; 43:1045-51.
Gagnon et al. *Acta Cytol.* 2004; 48:788-94.
Marchevsky et al. *Arch Pathol Lab Med.* 2006; 130:349-55.
Stewart et al. *Cancer Cytopathol* 2007; 111:203-9.

DIGITAL IMAGING PROCESS

- **Acquisition (e.g. capture)**
  - Liquid based cytology offers uniformly fixed & stained cellular areas relatively small to image.
- **Archiving (e.g. saving files)**
  - Entails image taxonomy & management.
- **Image manipulation (e.g. annotation)**
- **Image utilization (e.g. sharing)**
  - Imaged enhanced reports result in improved concordance between Pap tests & cervix biopsies.

Moriarty et al. *Cancer Cytopathol* 2007; 111:366.

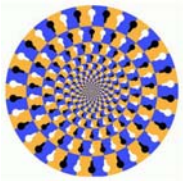
TODAY'S DIGITAL IMAGING DRAWBACKS

- Expensive initial set-up costs.
- Workflow interruption.
- Length of time to scan whole slides.
- Large storage size for WSI.
- Bandwidth restrictions.
- Undefined legal implications.
- Professional reluctance.
- Lack of standardization in the imaging process.
- Factors not unique to Cytology.

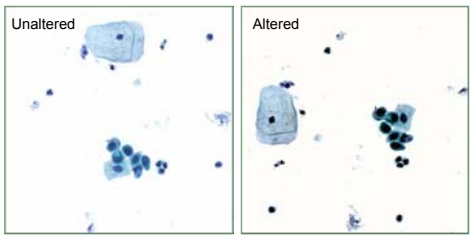
Impact of Digital Image Manipulation in Cytopathology

Arch Path Lab Med 2009; 133:57-61.

- **Manipulation of a digital image affects its interpretation.**
- **Care needs to be taken when digital cytology images are used, to specifically ensure that their alteration does not affect diagnosis.**
- **Standards related to the use of digital images in cytopathology are required to avoid the potential for misdiagnosis.**



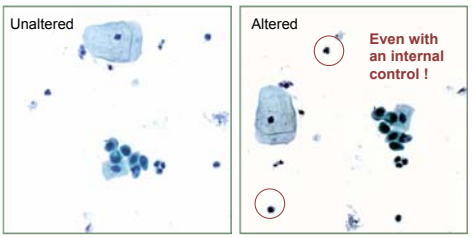
Manipulated Image



This particular image pair showed the least correlation in the study with the majority of the test takers overcalling the manipulated image HGSIL compared with the original image's diagnosis of negative.

Arch Path Lab Med 2009; 133:57-61.

Manipulated Image

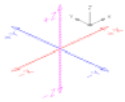


This particular image pair showed the least correlation in the study with the majority of the test takers overcalling the manipulated image HGSIL compared with the original image's diagnosis of negative.

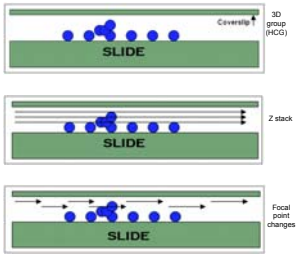
Arch Path Lab Med 2009; 133:57-61.

Factors Unique to Cytology

- Problem: 3D cell groups and thick smears.
  Dee et al. *Acta Cytol* 2007; 51:523-9.
- Solutions:
  Z-stack versus scanning at different focal planes (digital zoom, focal plane intercalation).

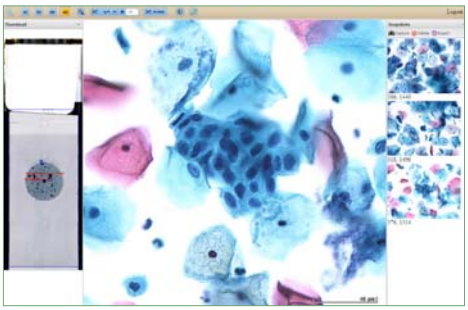


Z axis

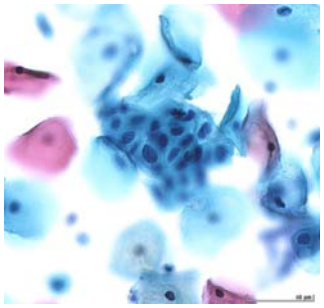


Multiplane images take long to scan (speed) & produce memory intensive files!

Virtual Image



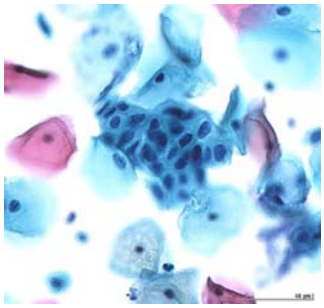
Virtual Focus



Z-level:

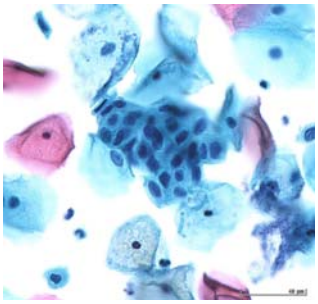
- 1µm

Virtual Focus



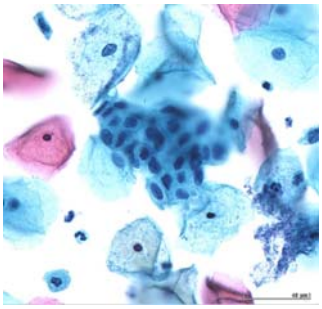
Z-level:
+ 1µm

Virtual Focus



Z-level:
+ 3µm

Virtual Focus

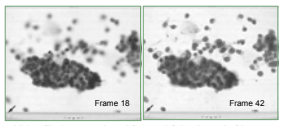


Z-level:
+ 5µm

Video Microscopy

Yamashiro et al. *Diagn Cytopathol* 2009; 37:727-31.

- **Microscope-mounted video cameras.**
- **Applications include:**
- **Conferencing.**
- **Telemicroscopy:**
  - **Dynamic.**
  - **Video images can improve "focusing" by playing files forward & backward.**



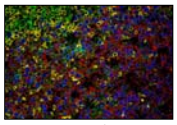
Video file images played forward & backward of breast cancer cells.

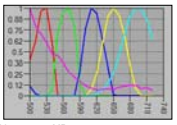
Case	Selected frame number
1	15, 14, 15, 15, 17
2	42, 42, 78, 42, 39
3	61, 56, 56, 55, 59
4	8, 25, 26, 24, 5
5	27, 34, 20, 24, 22
6	25, 24, 30, 26, 17
7	8, 9, 11, 15, 11
8	8, 12, 7, 10, 13
9	18, 17, 20, 26, 18
10	23, 21, 24, 22, 19

Selected frame numbers that were deemed to be representative images by video observers.

Emerging Imaging Methods

- **Multispectral image analysis:**
  - Utilizes spatial and spectral image information to classify images.
- **Image cytometry:**
  - Image-based measurement of cell properties.
- **Still investigational tools.**



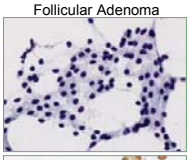
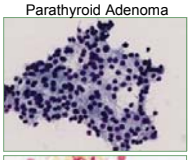
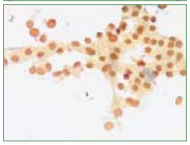
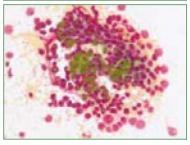


Images courtesy of RM Levenson, MD

Utility of multispectral imaging in differentiating lesions with subtle cytomorphologic differences

Mansoor et al. *Cancer* 2008; 114:22-6.

FNA

	Follicular Adenoma	Parathyroid Adenoma
Pap Stain		
Imaged cells with multispectral solution applied		

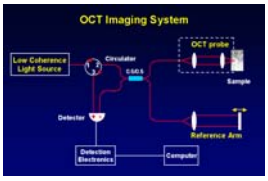
Pap Test Replacements

- **Growing literature highlights Pap test shortcomings (FNR).**
- **Direct cervix visualization of the cervix (“optical biopsy)**
  - e.g. digital cervicography
    optical coherence tomography
    speculoscopy (chemiluminescence)
- **Non-visual biophysical analyses**
  - e.g. Polarprobe (spectroscopic patterns)
- **Non-invasive but complementary (i.e. augment cytology) at best?**

Cervicography Digital Camera

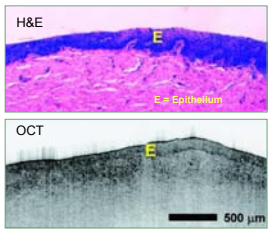
Spitzer M. *AJOG Reviews* 1998; 179:544-46.
Schneider & Zahm. *Ob Gyn Clin N Am* 1996; 23:657-73.

Optical Coherence Tomography

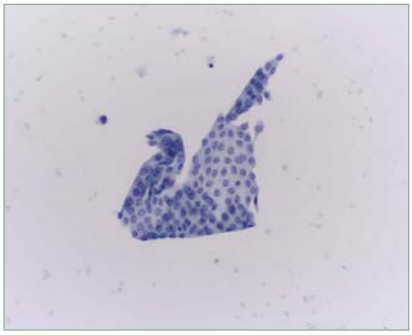


- **High-resolution cross sectional imaging.**
- **Resolution approaches the cellular range (1-15 micrometers).**
- **Analogous to US, but uses light instead.**

OCT Image of Cervix



Fujimoto JG et al. *Neoplasia* 200; 2:9-25.



4. AUTOMATED CYTOLOGY DEVICES

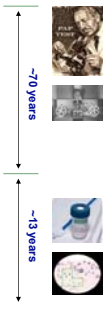
Linder J. *Arch Pathol Lab Med* 1997; 121:282-6

- **In 1996 only 12% of cytology labs were engaged in automated cytology.** Masood et al. *Diagn Cytopathol* 1998; 18:47-55.
- **Automated Preparation Devices**
  - **Cell collection from liquid samples, monolayer slide preparation, autostainers, etc.**
  - e.g. ThinPrep™ 2000 Processor, BD PrepMate™ Cell Enrichment Processor; MonoPrep® LBP Processor.
- **Screening Process Control**
  - **Computer interface with a microscope stage.**
  - **Ensures all fields on a slide have been examined.**
  - e.g. AcCell Series 2000, Pathfinder System, Cytosafe System.
- **Computer-Assisted Screening**

Computer-Assisted Screening

- **Manual Pap test screening is difficult, repetitive, labor-intensive, suffers from a significant FNR, carries ergonomic risk, & affected by screening environment.**
- **Compounded by skilled cytotechnologist shortage.**
- **Early semi-automated screening devices plagued by lack of a standardized process conducive to rapid acquisition and computer processing.**
- **Resulted in the advent of Liquid Based Cytology with a “monolayer”.**
- **Goal: Improved sensitivity, specificity & productivity over manual screening (that can consistently analyze slides around the clock without fatigue).**
- ***“Manual screening is an art & a science; Automated screening is more science than art !”***

Computer-Assisted Screening Timeline

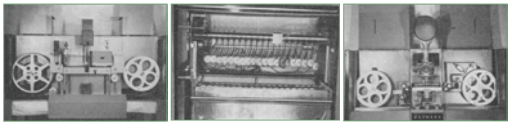


- **1923 – Papanicolaou (Pap) test introduced**
- **1928 – Pap test screening implemented**
- **1962 – Smear pattern recognition using a cytoanalyser**
- **1967 – Cytology screening apparatus using alcohol suspensions**
- **1983 – Early neural network (artificial intelligence) algorithms**
- **1995 – PAPNET™ System FDA approved for re-screening**
- **1996 – ThinPrep™ Pap test FDA approved**
- **1998 – BD FocalPoint™ Slide profiler (AutoPap 300 QC) FDA approved as a primary screening device with conventional smears**
- **1999 – Autocyte Prep™ (now BD SurePath™) Pap test FDA approved**
- **2001 – BD FocalPoint™ Slide profiler approved to screen SurePath™ slides**
- **2002 – ThinPrep Imaging System™ FDA approved**
- **2006 – MonoPrep™ Pap test introduced**
- **2008 – BD Focal Point™ GS Imaging System approved**

"Graphing Machine"

Brit Med J. 1967; 160-1

Automatic Preparation and Scanning in Cervical Cytology



Cell Writing Pen

A peristaltic pen in the centre deposits a line of cells on a transparent film strip as it passes.

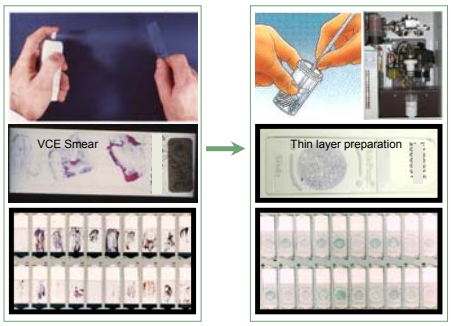
Staining Apparatus

The film strip is looped over a series of rollers. Below is a unit containing individual staining-baths that, when raised, immerse the rollers.

Viewing Apparatus

The prepared film on the left passes under the objective of a microscope (centre) for viewing on a screen or through binoculars.

LIQUID BASED CYTOLOGY



Fluid-Based Technology

Stoler MH. *Mod Pathol* 2000; 13:275-84

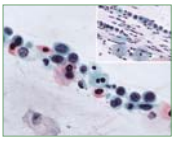
PROBLEMS SOLVED

- **Pre-analytic:**
  - Improved sampling, fixation, staining, background & fewer artifacts (e.g. overlapping cells).
  - Variables in slide quality are now under the control of the cytology laboratory.
- **Analytic:**
  - Smaller area on a slide to screen/image.
  - Monolayers easier to read.

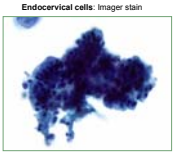
Trade Off

Endocervical cells: Prior to Imager stain

Conventional smear: HSIL in Mucus Strand



Endocervical cells: Imager stain



Liquid Based Pap: HSIL

NCI BETHESDA SYSTEM WEBSITE ATLAS

Automated Screening Systems

Pantanowitz et al. In: *Medical Informatics in Obstetrics and Gynecology*. 2009.

- **Primary screening systems**
  - **e.g. BD FocalPoint™ Slide Profiler (formerly AutoPap).**
  - **Self-contained onsite unit.**
  - **Slides scanned at varying objective levels.**
  - **Computer processors assign scores for each FOV.**
  - **Negative slides receive no human review & are archived.**
  - **Abnormalities require human review.**
- **Interactive screening systems**
  - **e.g. ThinPrep Imaging System™, BD FocalPoint™ GS Imaging System, MonoGen™.**
  - **Slide screening system scans the entire slide (e.g. 120 fields).**
  - **Data is processed using imaging algorithms.**
  - **Location guided workflow process ("pap map").**
  - **Cytotechnologist attention is driven using X-Y axis relocation to significant fields (e.g. 22 FOVs).**

Practical Issues

- **Imager inserted into workflow *(cytotech's cytotechnologist).***
- **Initial installation, calibration, & training.**
- **Abnormal fields may not be the most diagnostic.**
- **Specimen adequacy & diagnosis of infections limited to FOV.**
- **Reimbursement (billing) - CPT codes exist for both technical and professional components.**

Imaging Systems Outcomes

In General:

- Increase in abnormal Pap test diagnoses.
- Increase in pathologist-referred cases.
- Overall similar ASC-US HPV+ rates.
- Increased rates of biopsy-proven SIL detection.
- No change in HSIL Cyto-Histo correlation.

Published Message:

- Safe & effective technology that improves outcomes in patient care.
- Cost-effective in high volume cytology laboratories.
- Additional cost to the Pap test (a shift in labor cost from physician office to the lab, hardware, increased sensitivity with more cases for review).

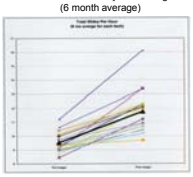
Cytotechnologist Productivity

- Initial learning curve.
- Increased cytotech productivity.
- Example of slide screening times:
  (Boost T. *Diagn Cytopathol* 2009; 37:661-4)

  Conventional smear = mean 5.6 min (10.7 slides/hour)

  TPI = mean 2.9 min (20.6 slides/hour)
- Need for new benchmarks & standards for cytotechnologist performance i.e. maximum workload limits (slides/hour).
- BD FocalPoint™ GS Imaging System = 170 slides/24 hour workload limitation.
- ThinPrep Imaging System™ = 200 slides/24 hour workload limitation

Total slides/hour for cytotechnologists
(6 month average)



Average increase of 2.2 slides/hour.
Pacheco et al. *Acta Cytol* 2008; 52:575-8.

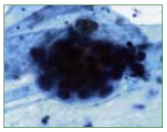
Imaging System Accuracy in Detecting Glandular Lesions

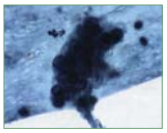
Jayamohan et al. *Diagn Cytopathol* 2009; 37:479-82.

- In a minority of cases, computer-assisted imaging devices fail to detect atypical/neoplastic glandular cells of interest within selected FOVs.
- Hence, there are reservations regarding total Pap test screening automation (i.e. without manual review).

Technology is not perfect, but neither is the Pap test, and nor are we.

AGCs missed by imaging



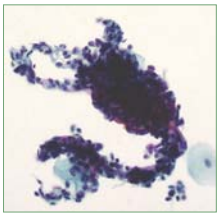


Malpractice Concerns

Skoumal & Cohen. *Diagn Cytopathol* 1996; 17:85-7.

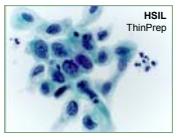
- Potential malpractice claims for automated screening imagers include:
  - Appropriate device QC
  - Personnel training
  - Compliance (e.g. with manufacturer standards)
  - ? Other

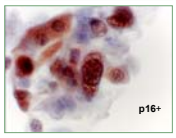
Are the IT vendors in our corner?



5. ANCILLARY TESTING

- Personalized medicine:
  Involves the use of molecular methods (information) to better manage a patient's disease or disease predisposition.
- Residual Pap vial & FNA material are available for ancillary testing.
- We should "seize the opportunity"!
  Clark DP. *Cancer Cytopathology* 2009; 117:289-97.
- Ancillary tests:
- HPV, immunocytochemistry, in-situ hybridization, molecular tests, etc.



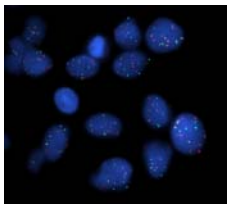


Images courtesy of C.N.Otis, MD

FISH & CHIPS

- Genetic alterations play an important role in cervix carcinogenesis.
- FISH assays are available for detecting gains (e.g. 3q & 5q) in cytology samples for risk stratification and triaging.

Seppo et *al. Gynecol Oncol. 114:80-3.*
Mian et al. *Gynecol Oncol.* 1999; 75:41-6.
Kurtycz et al. *Diagn Cytopathol.* 1996; 15:46-51.



FISH: Abnormal Cervical Pap

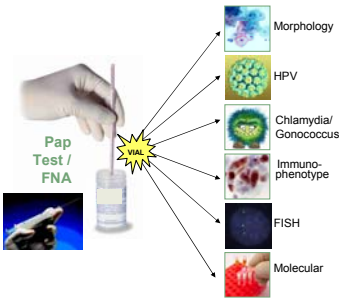
IT-related issues

- Hierarchy of ordering ancillary tests: (clinicians or the lab?).
- Handling specimens: Aliquots, split samples, & specimen tracking.
- Ordering: e.g. reflex testing.
- Data integration from disparate systems.

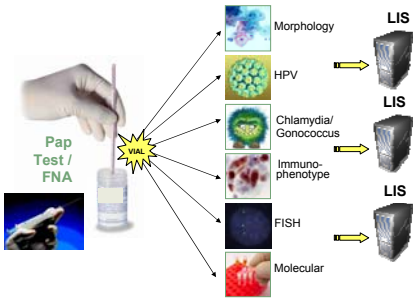
Vial of Information

Vial of Information

Vial of Information



Vial of Information



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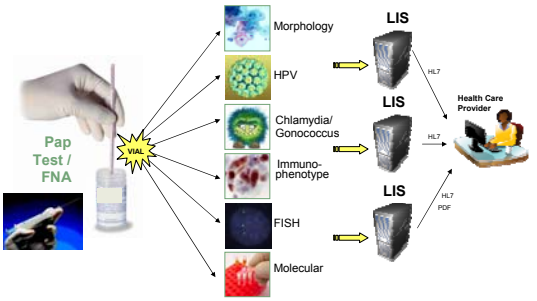


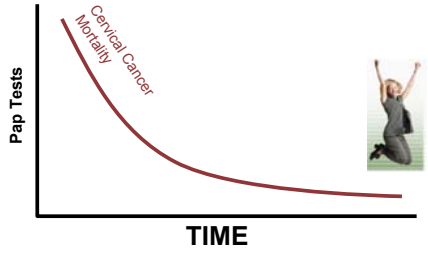
CONCLUSIONS
Where are we?

- Cytology has embraced informatics, particularly since CLIA '88.
- Ongoing utilization of LIS electronic databases for continuous QA/QC helps detect, correct, and reduce lab errors (akin to Clinical Pathology).
- Standardized diagnostic criteria & reporting are now expanding beyond GYN cytology.
- FDA approval has promoted the adoption of technology.
- Current digital applications include telecytology, automated Pap test screening, education & potentially proficiency testing.
- Telecytology, like telemedicine, is decentralizing practice.
- Automated Pap test screening has increased productivity & sensitivity.
- Technology is driving our quality monitors (e.g. workload limits, HPV rates). Professional organizations should play a role in developing standards.
- Liquid based cytology is helping meet demands for molecular testing.

Questions & Controversies
Where are we going?

- Are conventional Pap tests (smears) still considered acceptable standard of care?
- Is autoverification (no human review) of imaged abnormal Pap tests feasible?
- Will future re-screening require morphology review or molecular tests?
- Will automated screening be applied to non-GYN specimens and FNA biopsies?
- Once our images are in a computer system will they be outsourced?
- Are new technologies being incorporated into educational programs?
- Can we do it? i.e. keep cytologists in the center of clinical decision-making support?
- Can this technology help provide affordable cytology services in unscreened populations without an effective cytology infra-structure?
- Will disruptive technology (i.e. new technology that transforms markets) "replace" cytotechnologists &/or pathologists?

Is this what Dr Papanicolaou had intended?



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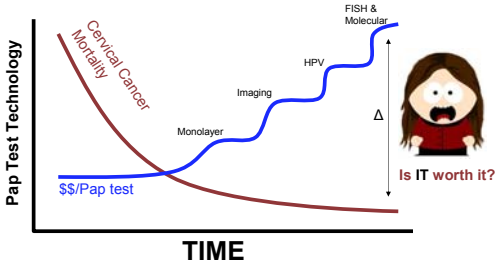
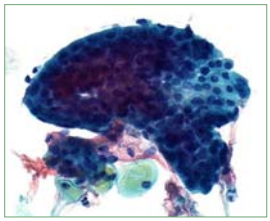


ACKNOWLEDGEMENT

- **Robert A. Goulart** MD
- **Maryanne Hornish** CT(ASCP), MBA