Poster Session

Presented in the
Grand Ballroom
Wyndham Grand Pittsburgh Hotel

Tuesday, May 24, 2016

10:20-11:20 am
And
3:35-4:00 pm

Listed in alphabetical order by
First Author

Application of Augmented Dickey Fuller Test for Identification of Systematic Error in Clinical Chemistry

Amir Momeni Boroujeni (amir.momeni@downstate.edu), MD[1], Elham Yousefi, MD[1], Aaron Harper, MD[1], Matthew Pincus, MD, PHD[2]

[1]SUNY Downstate Medical Center, Department of Pathology
[2]New York Harbor VA Medical Center

Content

The identification of systematic error is an important part of quality control in a clinical laboratory. The commonly used method to detect systematic error in analyte testing are the Westgard rules that require running at least two controls at least three times per 24h for each analyte tested; these can result in significant patient reporting delays if results on at least one control lies outside of 2 standard deviations from the cumulative mean. In this study we have tried a different approach for identifying systematic error that can potentially avoid time-consuming procedures.

Technology

We have utilized the Siemens Advia1800 Centralink 20, successive patient moving averages of potassium over a 6-month period for commonly ordered analytes (figure 1). We analyzed the data using R programming language.

Design

The quality control data for the same period including the high and low quality control results were also extracted. The average value of the low and high quality control was calculated and centered with patient averages. The patient averages and centered quality control averages distribution over a period of 30 days was compared using Kolmogorov-Smirnov (KS) test in order to validate the patient averages as a measure of quality control. The Augmented Dickey-Fuller (ADF) test was used to determine whether the patient averages time series is stationary over time. The final results were compared with the Levy-Jennings plots for the high and low controls over the same time period.

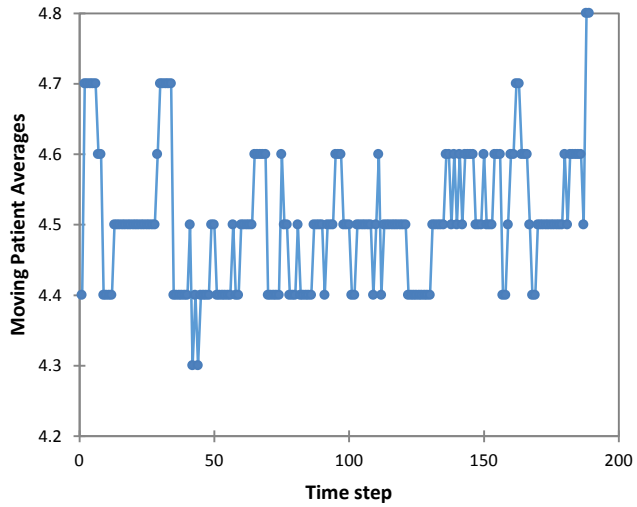
Results

The KS two-sample test had a p-value of 0.131 ($p<0.05$ indicating significant difference), showing the distributions are similar. The ADF test of the time series of moving patient averages of potassium levels is stationary with a value of -4.321 (critical cut off value for sample size: <-2.60). The Levy-Jennings plot of the quality control results in the same period did not show any systematic errors.

Conclusions

These results suggest that the ADF test of moving patient averages can be a strong tool in determining the presence or absence of systematic errors.

Figure 1. Time series showing the moving patient averages of potassium levels in a-month period



Differentiation of Invasive Melanoma from Dysplastic Nevi by Cell Graph Extraction of Melan-A Stained Slides

Amir Momeni Boroujeni (amir.momeni@downstate.edu), M.D.[1], Elham Yousefi[1], M.D., Motahareh Moghtadaei[2], PHD, Arash Momeni[2], PHD,
Alex Goncharuk[3], Viktor Goncharuk[4], M.D., David Mehregan[4], M.D.,Darius Mehregan[4], M.D.

[1]Dept. of Pathology, SUNY Downstate Medical Center, Brooklyn, NY
[2]Dept. of Biomedical Engineering, Dalhousie University, Halifax, NS, Canada
[3]Monroe County Community College, Monroe, MI
[4]Pinkus Dermatopathology Laboratory, Monroe, MI

Content
Dysplastic nevi are the most important differential of melanoma, both clinically and histologically, and can usually be reliably distinguished from melanomas using published criteria. In histologic review, differentiating the two entities is sometimes troublesome with some overlapping features. In this study we aim to apply computer analysis to distinguish these two entities.

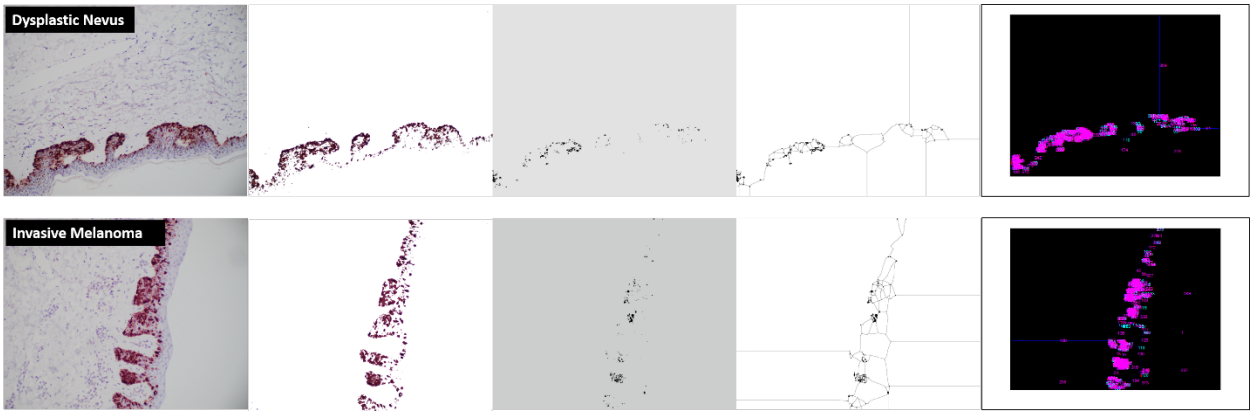
Technology
50 Melan-A stained glass slides each of invasive melanoma and dysplastic nevi were scanned at 200x magnification using Mikroscan technologies (Carlsbad, CA, USA) Q-Skan system.

Design
The resulting image stack for each glass slide was exported as a TIF image file. The images were thresholded using intermodes method and fed into the MATLAB based computer model. The model chose 5 regions of interest from each scanned slide, selecting ROIs that had the most uptake of the stain using image intensity processing. Each ROI was segmented using the Hierarchical K-means method and the resulting image was binarized and watersheded. The model then extracted the adjacency matrix representing the image and analysed the characteristics of the matrix (Figure 1). The network characteristics of 200 random ROIs were used to design a predictive model based on binary logistics regression and the remaining 300 ROIs were tested using the model.

Results
The most important predictors of the model were the number of isolated nodes, density and the number of components. The model was 96% accurate in differentiating the invasive melanoma ROIs from dysplastic nevi ROIs.

Conclusion
Our model has a very high accuracy in differentiating benign dysplastic nevi from malignant invasive melanomas. This model can be applied as a diagnostic aid for dermatopathologists in helping them diagnose melanocytic lesions with high degree of uncertainty.

Figure 1



Web Based Student Peer Evaluation System

Richard Lindquist, MD (Lindquist@uchc.edu)

University of Connecticut School of Medicine, Department of Pathology, Farmington, CT

Content

Medical student peer evaluation stimulates student participation in PBL, TBL & laboratory learning and improves group performance & learning. Moreover through peer evaluations students gain a discerning attitude toward their future colleges that is essential for optimum patient care. In order to facilitate peer assessments a web based peer evaluation system was developed

Technology

A web services solution stack consisting of Apache web server, MySQL database and PHP (hereinafter, web stack) was used to develop the Peer Evaluation System. Initially Uniform Server (http://www.uniformserver.com) and later Bitnami web stacks (https://bitnami.com/stacks) were employed. The Uniform Server, a Microsoft Windows operating system web stack, can run from a thumb drive or any USB storage device and requires no installation. Thus the system can simply be used on any Windows computer with a static IP address. The Bitnami web stack can run in Windows, Mac OS X or Linux environments as well as virtualized environments, and popular cloud platforms.

Design

Students presented with multiple checkbox list of potential peer reviewees selected their peers to review. On submitting the selected list, reviewers were presented with forms for each of their peers which allowed them to rank their peers for frequency, quality of peer interactions using radio buttons on a 1-5 basis. A text box was used for collecting written peer evaluation and the peer review was database stored. Programs allowed reviewees to see anonymously their reviews and aggregated ranking scores. Faculty programs generate summative evaluations as well as allowing drill down.

Results

The system has been designed, implemented and tested in classically run and flipped histology and pathology laboratories. Students have willingly accepted the use of the system; however, student evaluations have only been positive, never critical of their peers. This is in sharp contrast to student evaluation of their professors were student can be brutally critical.

Conclusions

In order to encourage student to be more discriminating in the peer evaluations 2 additional formats are being introduced to the system: divide the points and drag ‘n drop of rank order.

Web Based Student Response (aka Clicker) System

R.R. Lindquist, M.D.(lindquist@uchc.edu)

University of Connecticut School of Medicine, Department of Pathology, Farmington, CT

Content

A student response (aka clicker) system, which promotes active learning with increased student motivation and engagement, was developed for use in pathology and histology learning laboratories.

Technology

A web services solution stack consisting of Apache web server, MySQL database and PHP (hereinafter, web stack) was used to develop the clicker system. Initially Uniform Server (www.uniformserver.com) and later Bitnami web stacks (https://bitnami.com/stacks) were employed. The Uniform Server, a Microsoft Windows operating system web stack, is portable and can run from a thumb drive or any USB storage device. It requires no installation. Thus the system can simply be used on any computer with windows operating system and a static IP address. The Bitnami web stack can run in Windows, Mac OS X or Linux environments as well as VMware or VirtualBox virtualized environments, and popular cloud platforms such as Amazon Web Services (AWS), Microsoft Azure, Google Cloud Platform.

Design

A web based clicker system in conjunction with Aperio virtual microscopes (http://www.leicabiosystems.com/digital-pathology/aperio-digital-pathology-slide-scanners) was developed to actively engage first and second year medical students in pathology and histology laboratories. Using the digital conference feature of Aperio, lab preceptor by arrow or circle on the virtual slides asked students to select from a radio button list of possible answers for data base storage. Preceptors tracked student clicks and when complete the aggregated results were projected to the students for discussion. Programs allowed students to see at any time all of their responses and the corresponding correct response throughout the year. Faculty programs generate summative evaluations as well as allowing drill down.

Results

Student attitudes of the use of the web based clicker system in laboratory were very favorable and students looked forward to the continued use of the clicker system. Of 6 faculty who had the system available to them, 5 used it and employed it in writing summative student evaluations.

Conclusion

This web based clicker system engages students in pathology learning laboratories and leads to a student-centric learning experience.

Ultrasound Image Storage for Pathologist-Performed Ultrasound-Guided Fine Needle Aspiration

Sara E Monaco, Matt O'Leary, Jackie Cuda, Ralph Anderson, Liron Pantanowitz (pantanowitzl@upmc.edu)

University of Pittsburgh Medical Center, Department of Pathology

Content

With the introduction of pathologist-performed ultrasound-guided fine needle aspiration (USG-FNA), pathology departments are being challenged to manage Digital Imaging and Communications in Medicine (DICOM) images. We sought to incorporate such ultrasound images into our laboratory information systems (LIS) and picture archiving and communication system (PACS) to support our new USG-FNA practice.

Technology

BT12 LogiqE ultrasound machine (GE Healthcare). LIS (Cerner CoPath v3.2). *SimpleDICOM Receiver* and *Enterprise DICOM Wrapper* (developed by the University of Pittsburgh Medical Center). Networked workstation (HP computer, Intel Core, 8 GB RAM, Windows 7 Enterprise). PACS (iSite, Philips).

Design

Our FNA clinic started an USG-FNA service in 2015. Images form the portable ultrasound machine were uploaded into the LIS (with PicsPlus interface) using Universal Serial Bus (USB) flash drives, a customized DICOM Receiver, and via a shared folder on a networked workstation. JPEG images uploaded into the LIS were then automatically converted using an Enterprise DICOM wrapper and transmitted as DICOM files to a PACS server.

Results

Images (225 KB average file size) for 40 USG-FNA cases to date were uploaded into the LIS using USB flash drives (33 cases, 83%), our networked FNA clinic computer (5 cases, 12%), and DICOM receiver (2 cases, 5%). Table 1 compares all 3 image management methods. Using a shared network drive offered the highest quality images that could easily be incorporated into the LIS.

Table 1. Comparison of different methods to manage USG-FNA images.

Method of Archiving	Image File Management	Advantages	Disadvantages
USB flash drive	JPEG files manually removed from the US machine and manually uploaded to LIS	Cheap, portable and user friendly	Security (HIPAA) concerns, inability to use encrypted flash drives, and labor intensive
DICOM receiver	DICOM files transmitted directly from US machine to networked computer and manually uploaded to LIS as GIF files	Universal file format for radiology images	Low resolution images, small thumbnails, ambiguous file names, and difficult workflow
Networked workstation	JPEG files sent directly from US machine to networked computer and manually uploaded to LIS	Easiest workflow, with high-resolution images	Requires network access for US machine, and ambiguous file names

Conclusion

Pathology labs performing USG-FNA will likely need to manage their own ultrasound images, which is essential for radiological correlation, procedure documentation, billing and quality assurance. Saving these images as JPEG files in the LIS and DICOM format into a PACS is challenging. Our customized solution using a networked folder on the front end and DICOM wrapper for image conversion on the back-end works well.

Impact of Altering Image Parameters on Image Analysis Data Quality

Liron Pantanowitz(pantanowitzl@upmc.edu), MD[1], Chi Liu PhD[2], Yue Huang PhD[2], Huazhang Guo MD Phd[1], Gustavo K. Rohde PhD[2]

[1]Department of Pathology, University of Pittsburgh Medical Center
[2]Biomedical Engineering, Carnegie Mellon University

Content

The quality of data obtained from image analysis can be directly affected by several pre-analytical (e.g. staining, image acquisition), analytical (e.g. algorithm, region of interest) and post-analytical (e.g. computer processing) variables. Whole slide scanners generate digital images that may vary depending on the type of scanner and device settings. Our goal was to evaluate the impact of altering brightness, contrast, compression and blurring on image analysis data quality.

Technology

VL120 scanner (Omnyx). Visiopharm (Hoersholm, Denmark). MATLAB (2015a, MathWorks). Computer (Alienware/M14XR2, Intel i7 CPU 2.3GHz, 12G memory).

Design

Slides from 55 patients with invasive breast carcinoma were digitized to include a spectrum of HER2 scores analyzed with Visiopharm (30 cases with score 0, 10 with 1+, 5 with 2+, and 10 with 3+). For all images a region of interest was selected, and 4 parameters (brightness, contrast, JPEG2000 compression, out of focus blurring) then serially adjusted. HER2 scores were obtained for each altered image.

Results

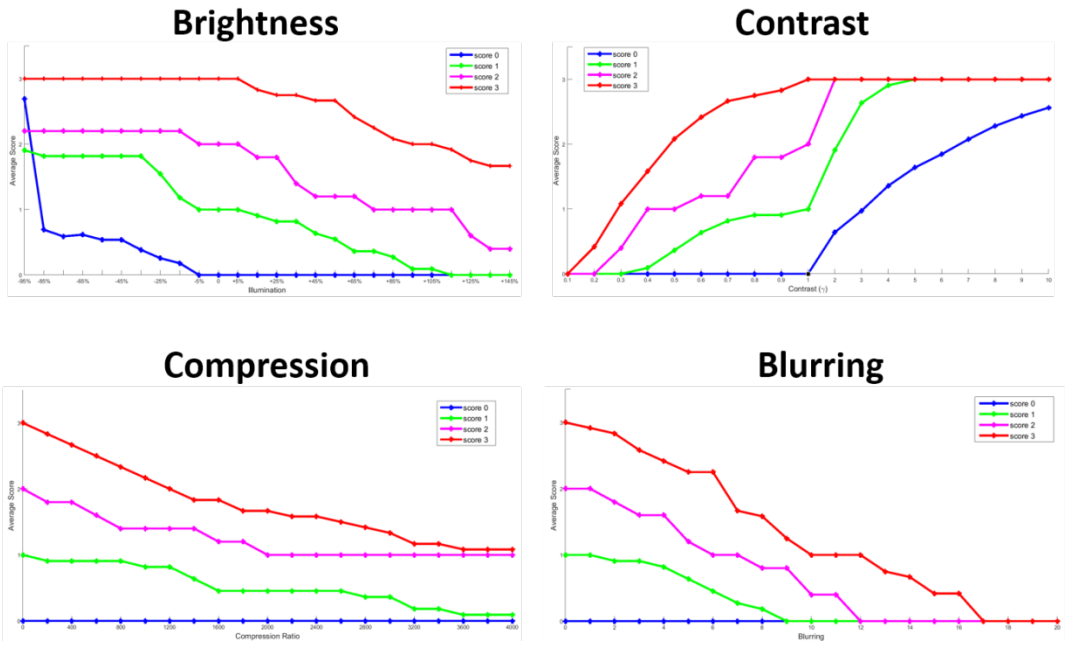
HER2 scores decreased with increased illumination, higher compression ratios, and increased blurring (see table 1 and figure 1). HER2 scores increased with greater contrast. Cases with HER2 score 0 were least affected by image adjustments.

Table 1. Impact of adjusting parameters on HER2 scores.

Parameter	Brightness	Contrast	Compression	Blurring
HER2 score change	Decreases with increased illumination	Increases with greater contrast	Decreases with higher compression ratio	Decreases with increased blurring
HER2 score with greatest impact	Score 1	Score 3	Score 3	Score 3
Value with least impact on HER2 score	±5%	Gamma: 1	Compression ratio: 200	Radius: 1 pixel

See next page for Figure 1.

Figure 1. Impact of altering image parameters on HER2 scores.



Conclusion

This experiment shows that variations in image brightness, contrast, compression and blurring can have major influences on image analysis results. Such changes can result in under- or over-scoring with image algorithms. Standardization of image analysis is recommended in order to minimize the undesirable impact such variations may have on data output.

Pathology Informatics Essentials for Residents (PIER): Outcome of Alpha Testing by Pathology Resident Training Programs

Liron Pantanowitz (pantanowitzl@upmc.edu), MD[1], Walter H. Henricks MD[2], Donald S. Karcher MD[3], Priscilla Markwood[4], Ann Neumann PhD[5], Kristen Johnson PhD[5], Amanda Lofgreen MS[5], Trish Glover BSN MS[5], Sue Plath MA[5]

[1]Department of Pathology, University of Pittsburgh Medical Center
[2]Center for Pathology Informatics, Cleveland Clinic
[3]Department of Pathology, The George Washington University
[4]Association of Pathology Chairs
[5]CAP Learning, College of American Pathologists

Content
The PIER pathology informatics curriculum (Release 1) was launched in September 2014 to facilitate training of U.S. pathology residents. PIER materials were made freely available to all pathology residency programs (http://www.apcprods.org/pier/). To evaluate PIER and support adoption, a group of pathology resident training programs were selected to alpha test the curriculum. Our aim is to report the findings of this testing.

Technology
Feedback was gathered via online surveys (SurveyMonkey®), phone interviews, and virtual focus groups (Citrix GoToWebinar).

Design
12 programs that represented a cross-section of program sizes, geographic locations, and levels of informatics expertise, were selected in the alpha test. Feedback was solicited on four occasions between November 2014 and October 2015 from the department chair, program director, faculty and residents. Nine non-alpha programs also implementing PIER during this time provided input via online survey.

Results
In total, seven department chairs, 30 implementers (program directors and faculty), and 82 residents provided feedback. Programs that already had an informatics curriculum agreed that PIER improved their training (average rating = 4.46, 5-point scale). Most programs without an informatics curriculum agreed that PIER effectively supported implementing informatics training (average rating = 3.87), and had a positive impact on learning. On average, residents reported significant increases in their knowledge/skill after PIER was implemented. 46% of implementers found implementing PIER to be more difficult than other curriculum changes their programs had made; 32% found it easier and 21% found it about the same. Similar to other curriculum changes, the greatest reported challenges were lack of time and/or faculty expertise. The majority (86% chairs, 79% implementers) reported that they were likely to continue using PIER.

Conclusions
The findings from the alpha test indicate that: (1) the PIER curriculum and associated tools are effective, (2) participating residents reported an increase in knowledge/skill related to PIER learning objectives, (3) implementing PIER may be more difficult than other curriculum changes, and (4) despite implementation difficulties, most participants support PIER and would recommend it to other programs.

Image Analysis Using Shape-Based Modeling Segmentation to Grade Renal Cell Carcinoma

Liron Pantanowitz (pantanowitzl@upmc.edu), MD[1], Thomas Martel MSEE[2], John T. Freyhof MBA[2]

[1]Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA
[2]CytoSavvy, Wayne, PA, USA

Content

Several technologies are available to create image analysis algorithms for diagnostic use in pathology. One approach is to employ symbolic object model technology that targets edge detection, in order to generate a database of shape and identity metadata for elements of each image. Our aim was to test whether such shape-based modeling segmentation could be used to develop an image algorithm to automate the grading of renal cell carcinomas.

Technology

CytoSavvy image analysis technology utilizing Bézier curves (up to cubic order) and Ellipse object models. Multiple threshold, multiple resolution dashboard to display image data (https://www.cytosavvy.com/renal-tumor-grading-dashboard.html).

Design

Digital slides of renal cell carcinoma cases with varying grade were selected. These whole slide images were used to develop a set of algorithms, collectively called shape-based modeling segmentation, to grade these tumors. Decision-tree logic was applied to identify cells and multicellular structures based on an extensive morphology database. The algorithm conformed to Fuhrman nuclear grades (1 to 4) using criteria (nuclei size, nuclear shape, presence of nucleoli) outlined in the kidney AFIP Atlas of Tumor Pathology. Analyzed data was displayed in a browser-based interactive dashboard (Figure 1).

Results

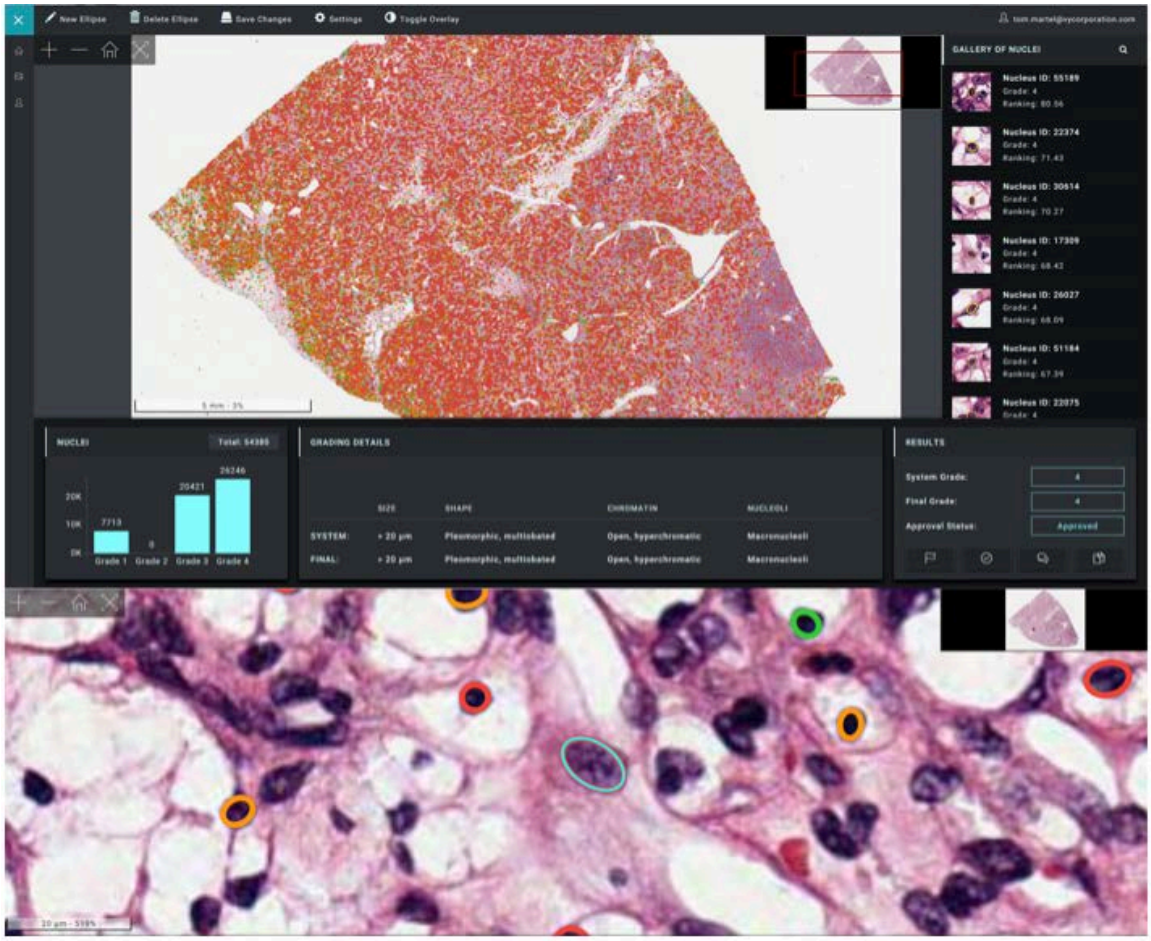
The algorithm reliably identified renal carcinoma nuclei and automatically generated an overall Fuhrman nuclear grade. For each tumor, an overview heat map showing heterogeneity of nuclear grade was established. The dashboard provided the exact number of nuclei/grade present for the entire slide and an image gallery of all individually graded nuclei for verification.

Conclusion

We successfully developed an image algorithm using shape-based modeling segmentation to automatically grade renal cell carcinoma from whole slide images, and a web-based solution for efficient workflow that displays analyzed data. Future work is aimed at clinical validation of this algorithm and applying the same technology to automate grading and scoring of other tumor types.

See Figure 1 on next page

Figure 1. CytoSavvy interactive dashboard (top panel) and highlighted automated nuclei detection (bottom panel).



Whole Slide Imaging (WSI) Consistency: A Multinational Approach

Eric Vail, MD (eric.vail@wmchealth.org)[1] , Daiki Taniyama, MD[2], Kiyomi Taniyama MD[2], Kazhiro Tabata MD[3], Junya Fukuoka MD[3], Ichiro Mori MD[4], Robert Y Osamura MD[4], John Fallon MD PhD[1], Yukako Yagi, PhD[5]

[1]New York Medical College at Westchester Medical Center
[2]National Kure Medical Center and Chugoku Cancer Center, Japan
[3]Nagasaki University, Japan
[4]International University of Health and Welfare Hospital, Japan
[5]Massachusetts General Hospital

Content
WSI is a rapidly emerging field in pathology and current efforts are under way to obtain FDA approval for primary diagnosis. It is critical that scanners in different locations produce the same result from the same slide. We evaluated system variability between multiple scanners of the same type at multiple locations.

Technology
Five Phillips Ultra Fast Scanners and five Hamamatsu Nanozoomers were used. All scanners were currently commercially available, unmodified, high volume, high speed scanners.

Design
Fifteen slides were selected for scanning on individual scanners in ten different locations. The slides were assessed for quality and discrepancy between their respective images. A grading system including color, focus and reproducibility was devised to determine if the image was of acceptable quality or required rescanning.

Results
The number of slides that needed rescanning, averaged 2 out of 15 (13%). All of the unacceptable scans had one or more, less than one square millimeter areas that were out of focus. The specific focus abnormalities were not present on rescanned images. All 5 of one scanner type consistently failed to recognize two levels on one of the slides across all of the sites. After discussion with the vendor a tentative fix was made. One scanner had multiple focus discrepancies. However, after maintenance was performed, its performance conformed to the rest of the group. Color discrepancies were site specific and correlated with time from last calibration and software version.

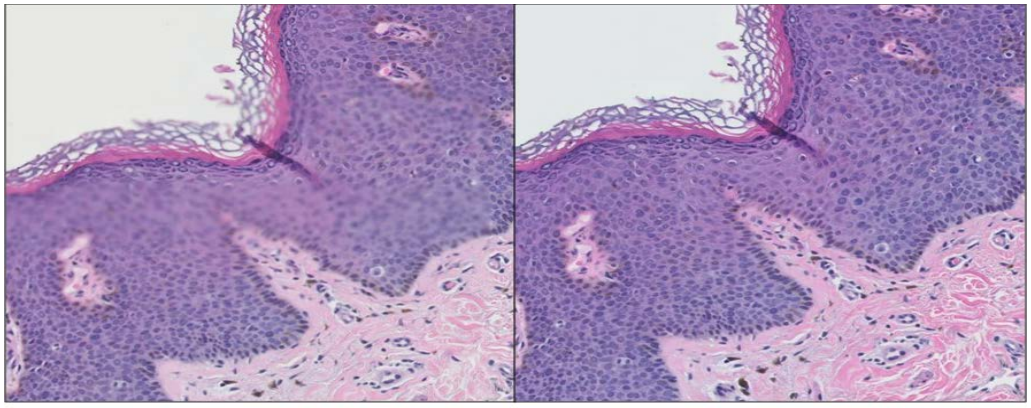


Figure 1:
Example of an area of focus discrepancy between two images

Conclusion
Our findings show that currently the machines that we tested showed few variances in slide image quality. The areas that were out of focus were unique to the scanner tested and comparatively small. We did not see any scanning error that disrupted diagnosis. We also found that a large number of levels on one slide presented challenges for the tissue recognition for one of the scanner types. Individual scanners had noticeable inter-site color variation, but no intra-site discrepancies. This was correlated with calibration history and software version. Standardization of image quality evaluation protocol and scanner consistency is critical for continued evolution of diagnostic WSI capabilities.

Provider and Patient Acceptance of Auto-release of Test Results

Jennifer S. Woo MD[1] (jswoo@mednet.ucla.edu), Opal Reddy MD[1], Thomas A. Drake MD[1]

[1]David Geffen School of Medicine at UCLA, Department: Pathology and Laboratory Medicine

Content
CMS meaningful use stipulates that patients are provided timely online access to their health information. We report experience of a large health system in meeting this goal with regard to lab results through implementation of an auto-release policy on a patient portal, with a specific assessment of tumor markers for Hematology-Oncology patients.

Technology
Epic 2014 is the electronic health record system in place at the time of this assessment, with the MyChart feature as the patient portal. Data for the numbers of cancer antigens tests were obtained from the Epic Clarity data repository.

Design
This is a descriptive study of acceptance of auto-release of laboratory data through the patient portal over a 13 month period, beginning Oct 2014. Patient and physician experience were known through monthly meetings and reports from the MyChart team. Test data were obtained for the cancer antigen markers CA125, CA15-3, CA19-9, and CA27.29.

Results
The vast majority of lab tests results were auto-released 3 days after resulting. Tests excluded from auto-release because of California law were pathology results, and tests related to HIV, hepatitis, and drugs of abuse. Also excluded were genetic tests. Since implementation, the MyChart committee received only one formal request to change lab release policy. This was from a Hematology-Oncology clinician, responding to a patient complaint related to cancer antigen tests. To obtain context for this, cancer antigen test ordering was assessed. A total of 21,881 cancer antigen tests were ordered for 5,631 patients, the majority being ordered by specialists (75% of total). A third of test values were deemed as elevated. These data supported continuing current policy.

Conclusions
Access to personal health information empowers patients to engage their health care. The vast majority of patients embrace this, but on occasion the auto-release of certain tests before the ordering physician is able to effectively communicate results, leads to patient distress. Currently any given test is auto-released or not to all patients. Enabling personalized auto-release of test results could mitigate this issue.

Quantitative phase imaging to improve the diagnostic accuracy of urine cytology

Hoa V. Pham (hvp2@pitt.edu)[1]; Liron Pantanowitz[2]; Yang Liu[1]

[1]Departments of Medicine and Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania
[2]Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Content
Definitive diagnosis of urothelial carcinoma in urine specimens based on cytomorphology alone may be challenging, with 30% “indeterminate” diagnosis. We present the use of quantitative phase imaging (QPI) to quantify the nuclear dry mass of unstained urine cytology specimens to improve the diagnostic accuracy of urine cytology.

Technology
QPI is an emerging technology in which quantitative phase images of unstained specimen can be obtained, from which the dry mass can be accurately measured at single cell and nucleus level. A custom-built quantitative phase microscope was used, which provides a high-contrast low-noise quantitative phase image from unstained cells.

Design
Urine samples were processed with ThinPrep, and unstained slides were made. Urothelial cells from four categories of cytological diagnosis (negative, atypical, suspicious, positive) were imaged and three parameters (nuclear dry mass, nucleus-to-cytoplasm dry mass ratio, nuclear entropy) were calculated for each cell (~50-400 cells per patient). A multivariate scoring scheme with each parameter tested against a chosen threshold resulting in a TRUE or FALSE outcome. A diagnosis for each patient was based on majority vote of the three outcomes.

Results
Quantitative analysis of the nucleus dry mass showed a progressively higher value for the four diagnostic categories, with morphologically benign and malignant urothelial cells well separated, and the atypical and suspicious cases also showing significant differences. **Table 1** shows our prediction results with the initial and clinical follow-up diagnosis, which shows a perfect match with the patients’ available follow-up.

Conclusion
QPI shows potential to improve the diagnostic accuracy of urine cytology, based on precise quantitative assessment of nuclear dry mass in label-free cells. A large-scale study is needed to verify this scoring scheme as well as to train the test thresholds to get a rigorous diagnostic scoring scheme.

See next page for Table 1.

Table 1. Proposed QPI based scoring scheme for cytologic diagnosis (NC: Nuclear dry mass; NE: nuclear entropy, NCMR: nuclear to cytoplasm dry mass ratio)

Case Number	Cytology Diagnosis	Follow-up histology (or urine)	Tests			Our Results
			NC > 21pg	NE > 0.62	NCMR > 0.5	
1	Atypical	None	1	1	0	**1**
2	Atypical	Urothelial carcinoma in situ	1	1	0	**1**
3	Atypical	None	0	0	0	**0**
4	Atypical	Papillary urothelial carcinoma HG non-invasive	1	1	0	**1**
5	Atypical	Benign (inflammation)	1	0	0	**0**
6	Normal	(Negative)	0	0	0	**0**
7	Normal	(Atypical)	0	0	0	**0**
8	Normal	None	0	1	0	**0**
9	Normal	(Negative)	0	0	0	**0**
10	Suspicious	HG urothelial carcinoma	1	1	0	**1**
11	Positive	HG urothelial carcinoma	1	1	1	**1**
12	Suspicious	HG urothelial carcinoma	1	1	0	**1**
13	Suspicious	Urothelial carcinoma in situ	1	1	0	**1**
14	Positive	Urothelial carcinoma in situ	1	1	1	**1**
15	Suspicious	(Suspicious)	1	1	1	**1**
16	Positive	(Positive)	1	1	1	**1**
17	Positive	HG urothelial carcinoma	1	1	1	**1**
18	Positive	Ureter mass (developed metastastic bladder cancer)	1	1	1	**1**
19	Suspicious	HG urothelial carcinoma	1	1	1	**1**
20	Atypical	LG papillary urothelial carcinoma	1	1	0	**1**
21	Atypical	HG urothelial carcinoma	1	1	0	**1**
22	Atypical	HG urothelial carcinoma	0	1	1	**1**
23	Atypical	(Atypical)	0	0	1	**0**
24	Positive	HG urothelial carcinoma	1	1	1	**1**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